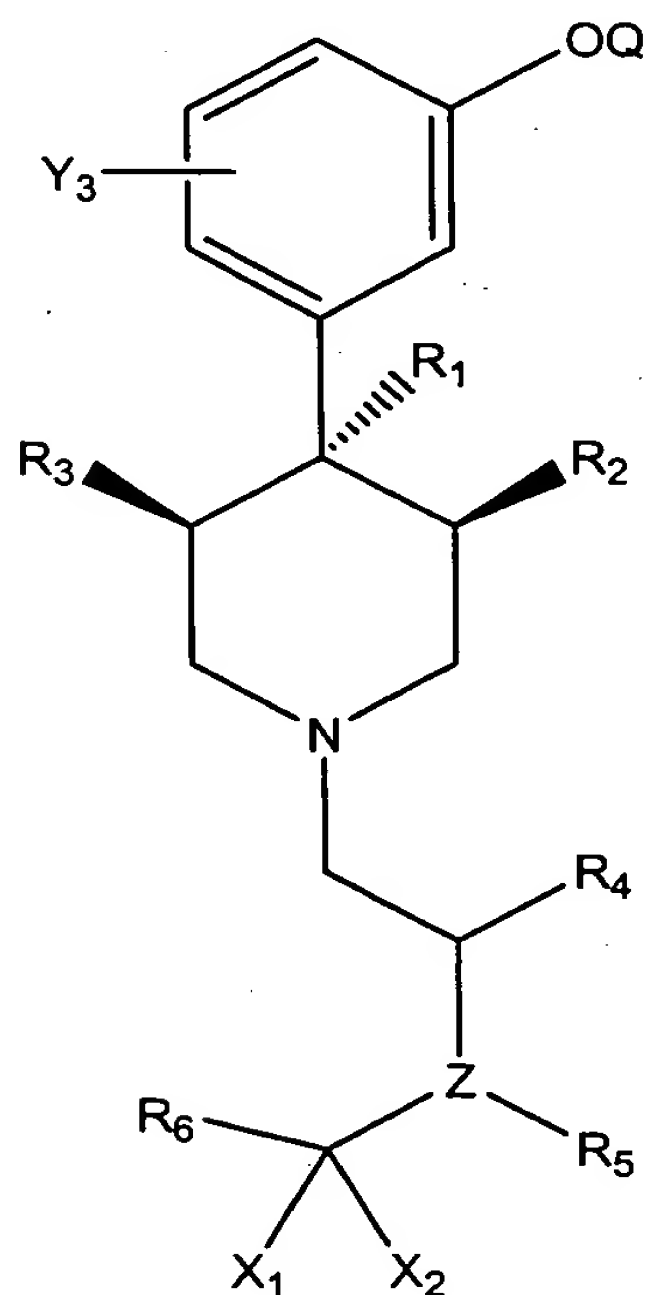


CLAIMS

Please amend the claims as follows:

Claim 1 (Currently Amended): A method of binding a kappa opioid receptor in a subject in need thereof, comprising:

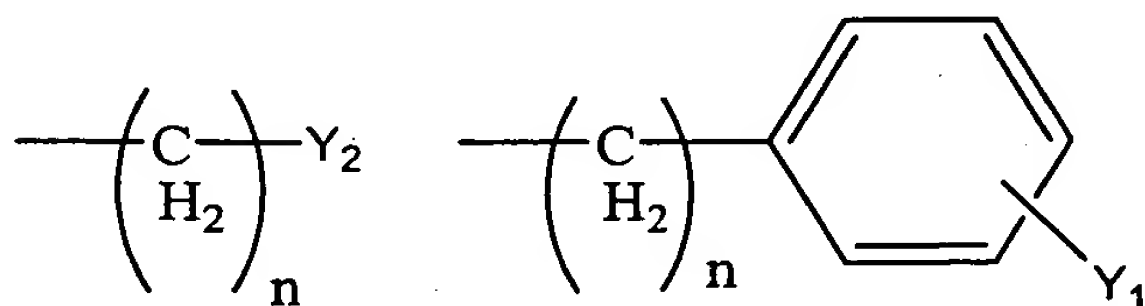
administering to said subject a composition comprising a kappa opioid receptor antagonist and a physiologically acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula (1):

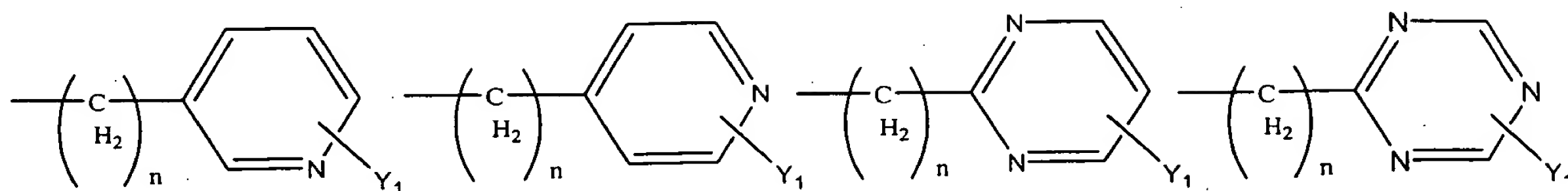


(I)

wherein Q is H or COC<sub>1-8</sub> alkyl;

R<sub>1</sub> is C<sub>1-8</sub> alkyl, or one of the following structures:





$Y_1$  is H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $OR_8$ ,  $CO_2R_9$ ,  $C_{1-6}$  alkyl,  $NR_{10}R_{11}$ ,

$NHCOR_{12}$ ,  $NHCO_2R_{12}$ ,  $CONR_{13}R_{14}$ , or  $CH_2(CH_2)_nY_2$ ;

$Y_2$  is H,  $CF_3$ ,  $CO_2R_9$ ,  $C_{1-6}$ alkyl,  $NR_{10}R_{11}$ ,  $NHCOR_{12}$ ,  $NHCO_2R_{12}$ ,  $CONR_{13}R_{14}$ ,

$CH_2OH$ ,  $CH_2OR_8$ , or  $COCH_2R_9$ ;

$Y_3$  is H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $OR_8$ ,  $CO_2R_9$ ,  $C_{1-6}$  alkyl,  $NR_{10}R_{11}$ ,

$NHCOR_{12}$ ,  $NHCO_2R_{12}$ ,  $CONR_{13}R_{14}$ , or  $CH_2(CH_2)_nY_2$ ;

$R_2$  is H,  $C_{1-8}$  alkyl,  $C_{3-8}$  alkenyl,  $C_{3-8}$  alkynyl or  $CH_2$ aryl substituted by one or more groups  $Y_1$ ;

$R_3$  is H,  $C_{1-8}$  alkyl,  $C_{3-8}$  alkenyl,  $C_{3-8}$  alkynyl or  $CH_2$ aryl substituted by one or more groups  $Y_1$ ;

wherein  $R_2$  and  $R_3$  may be bonded together to form a  $C_{2-8}$ , alkyl group;

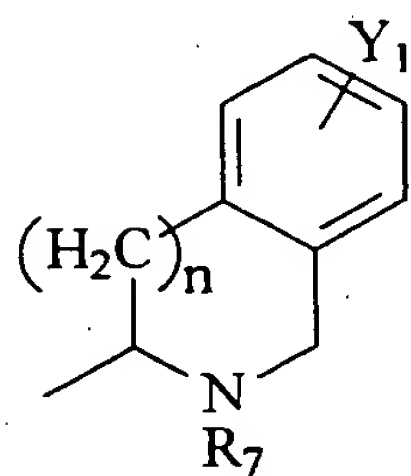
$R_4$  is hydrogen,  $C_{1-8}$  alkyl,  $CO_2C_{1-8}$  alkylaryl substituted by one or more groups  $Y_1$ ,  $CH_2$ aryl substituted by one or more groups  $Y_1$  or  $CO_2C_{1-8}$  alkyl;

$Z$  is N, O or S; where  $Z$  is O or S, there is no  $R_5$

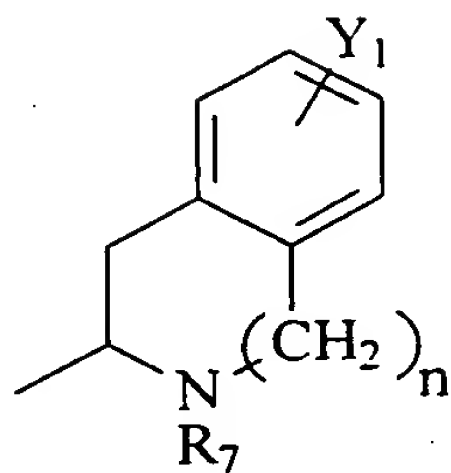
$R_5$  is H,  $C_{1-8}$  alkyl,  $C_{3-8}$  alkenyl,  $C_{3-8}$  alkynyl,  $CH_2CO_2C_{1-8}$  alkyl,  $CO_2C_{1-8}$  alkyl or  $CH_2$ aryl substituted by one or more groups  $Y_1$ ;

$n$  is 0, 1, 2 or 3;

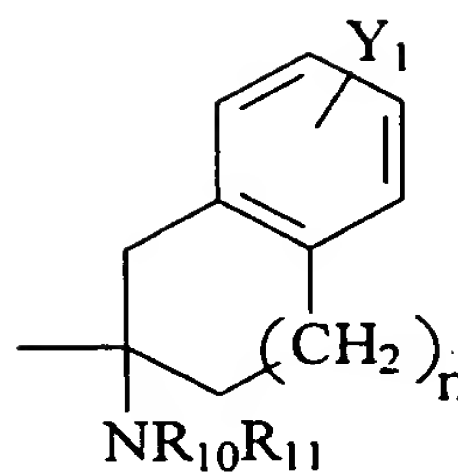
$R_6$  is a group selected from the group consisting of structures (a)-(bbb):



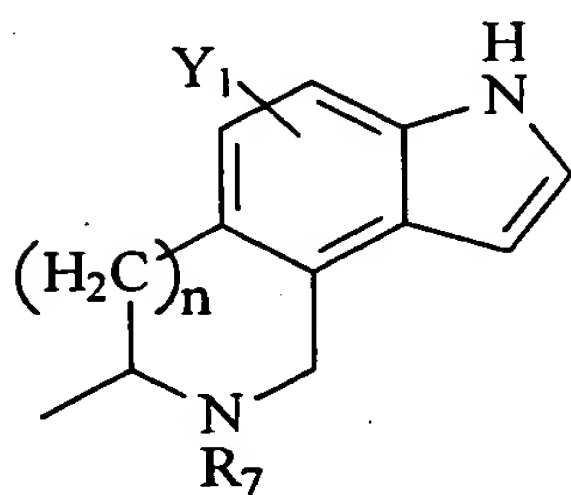
(a)



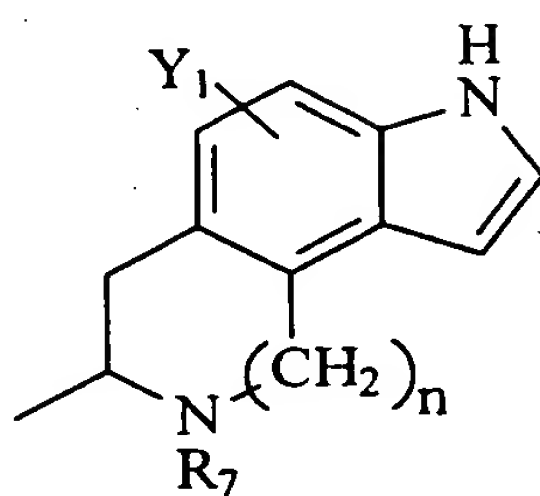
(b)



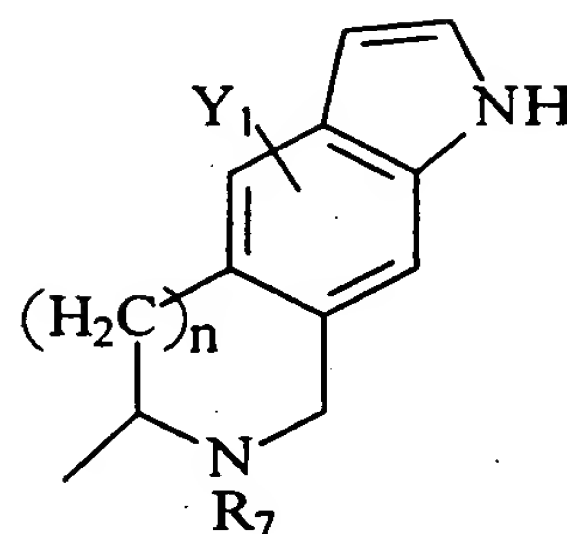
(c)



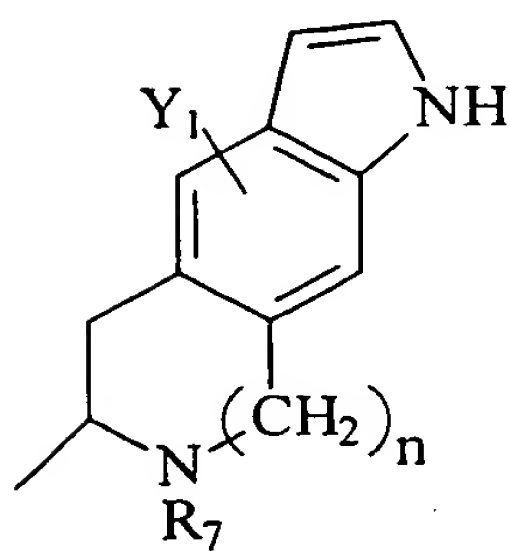
(d)



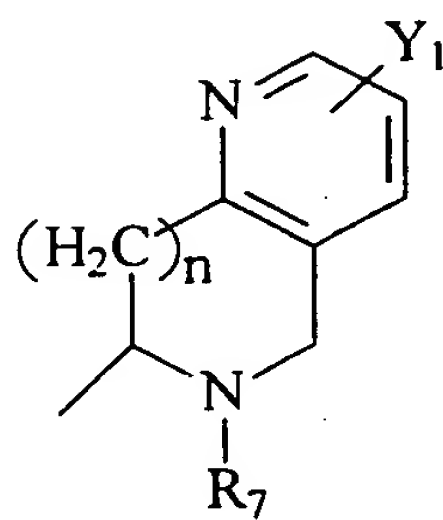
(e)



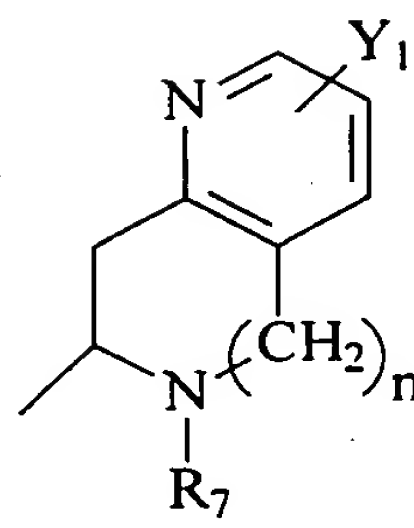
(f)



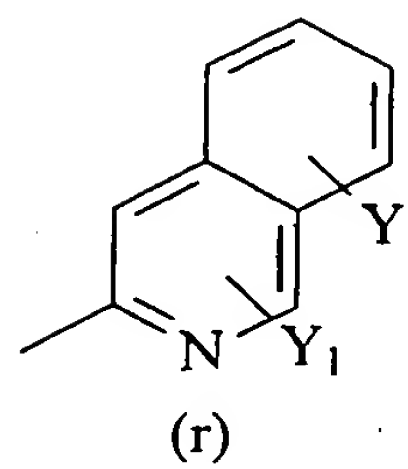
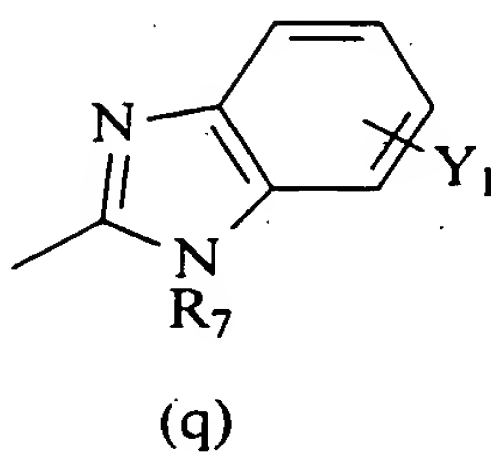
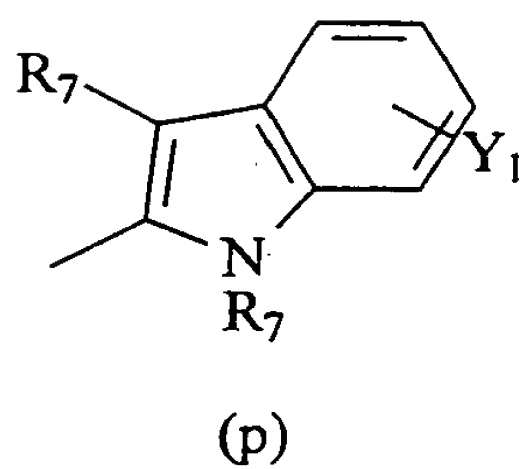
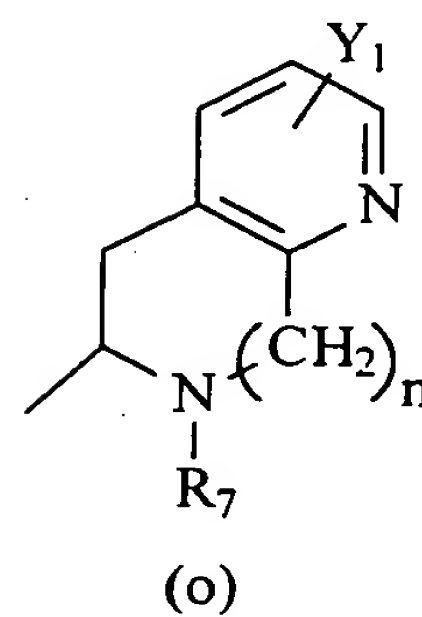
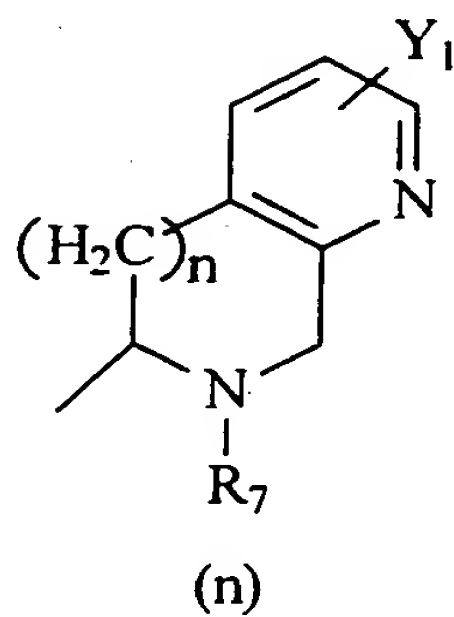
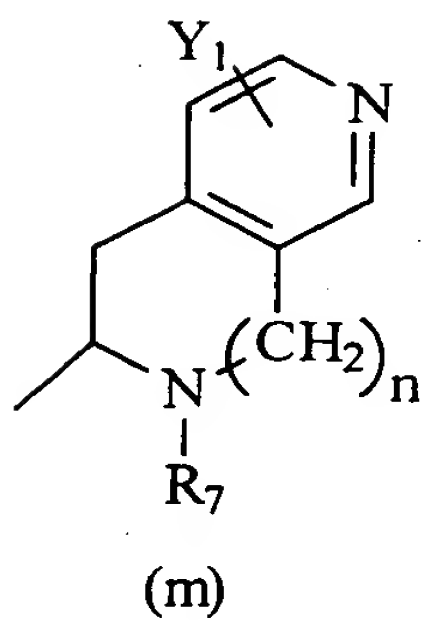
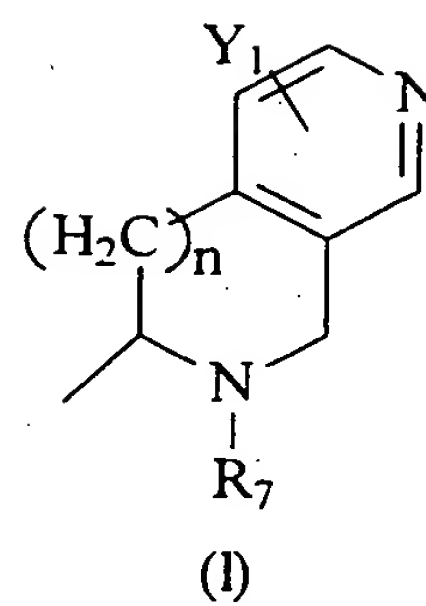
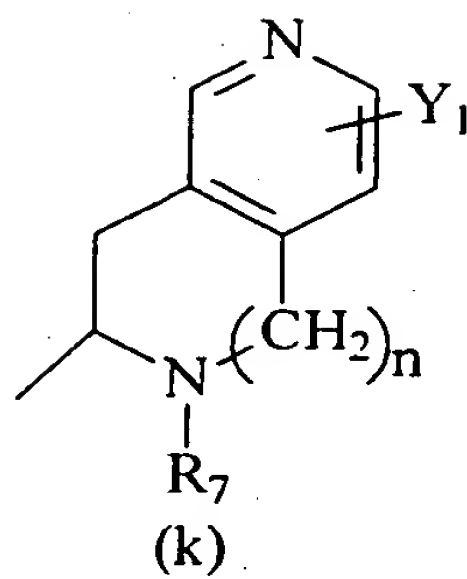
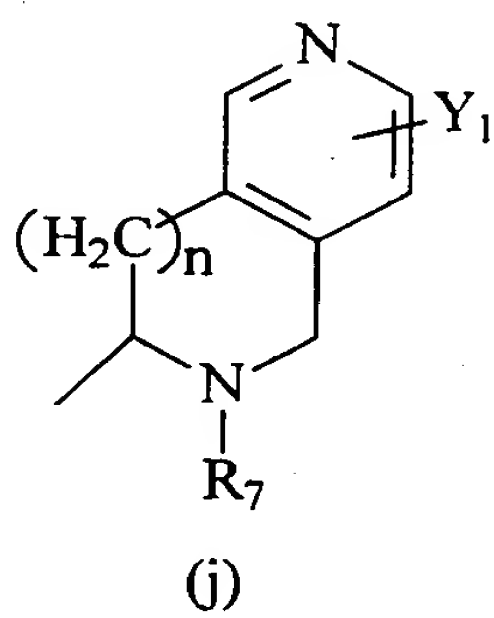
(g)

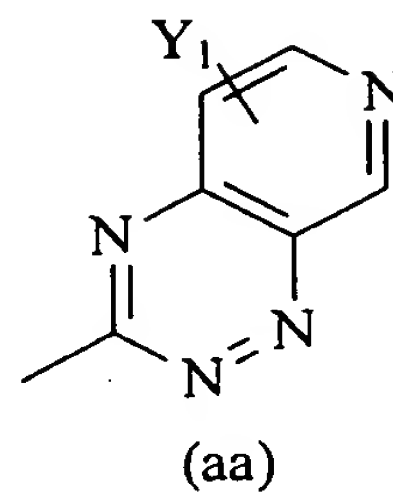
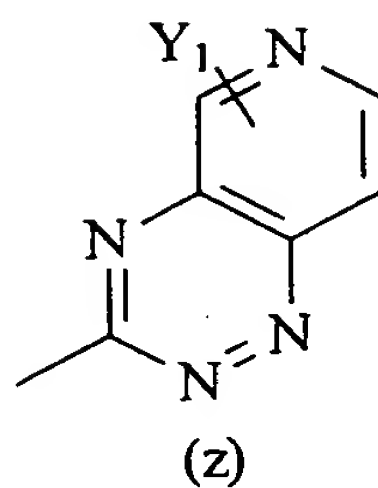
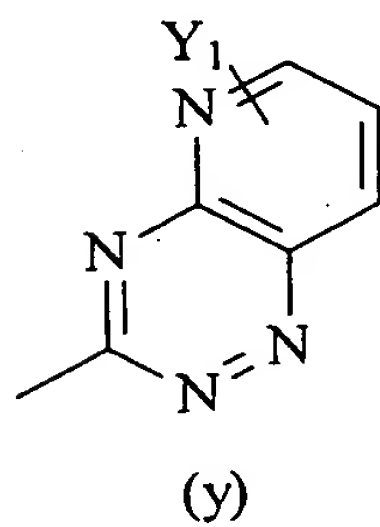
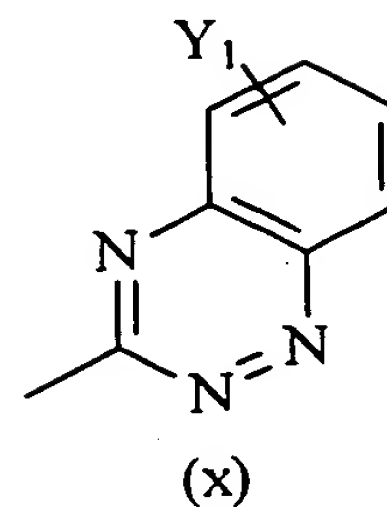
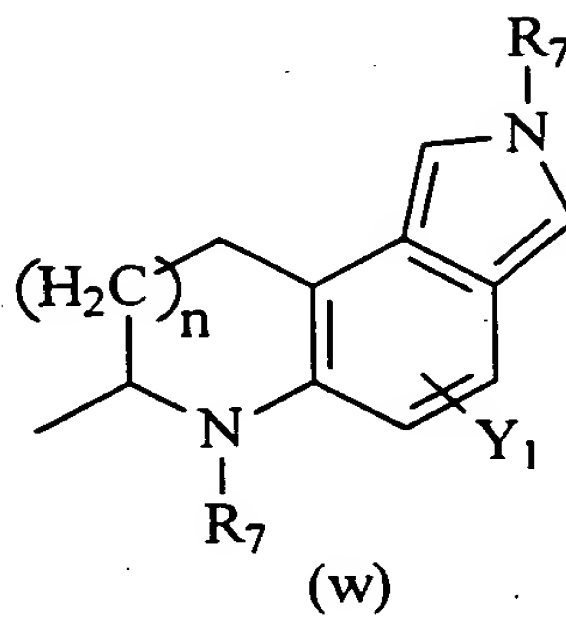
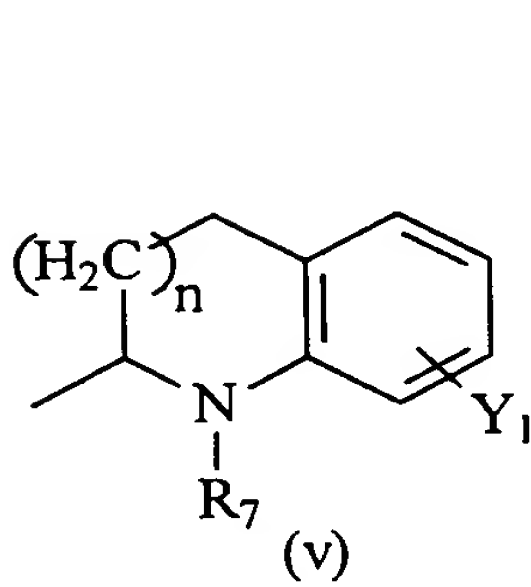
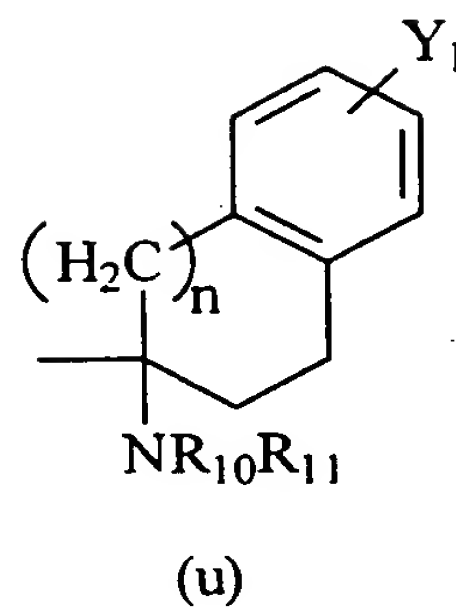
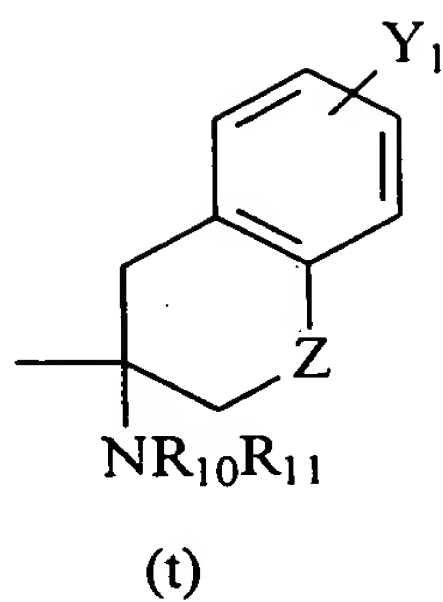
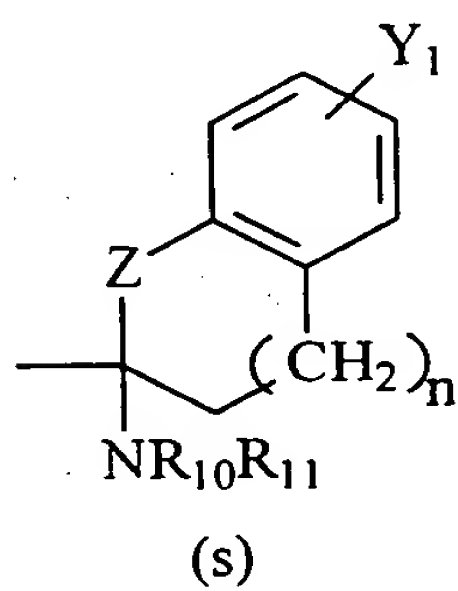


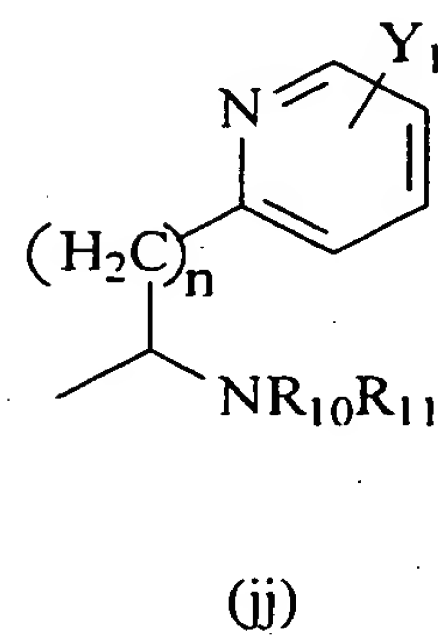
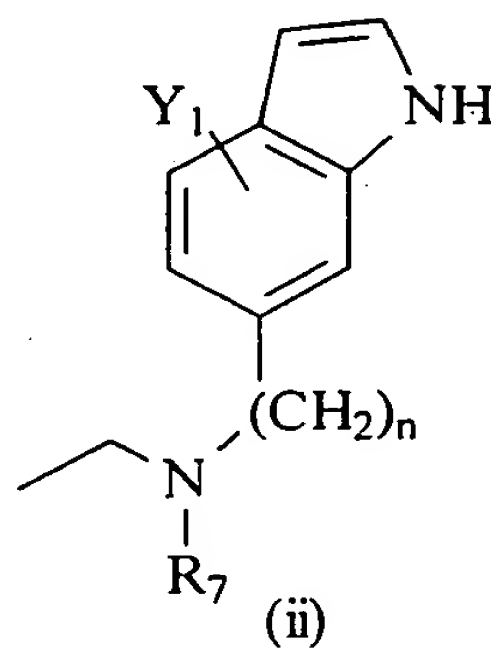
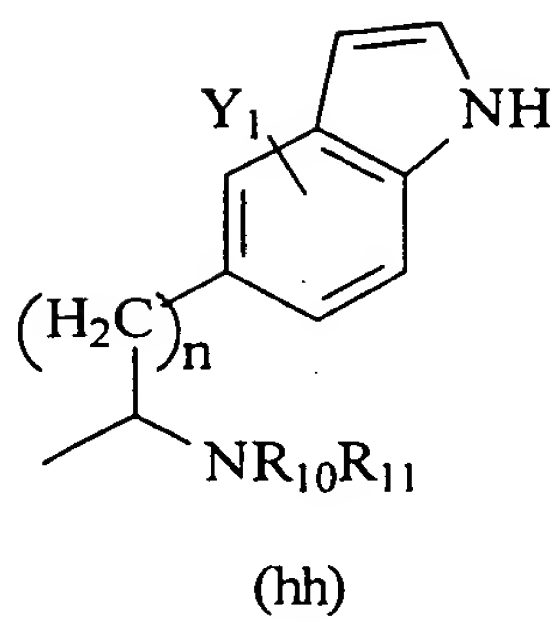
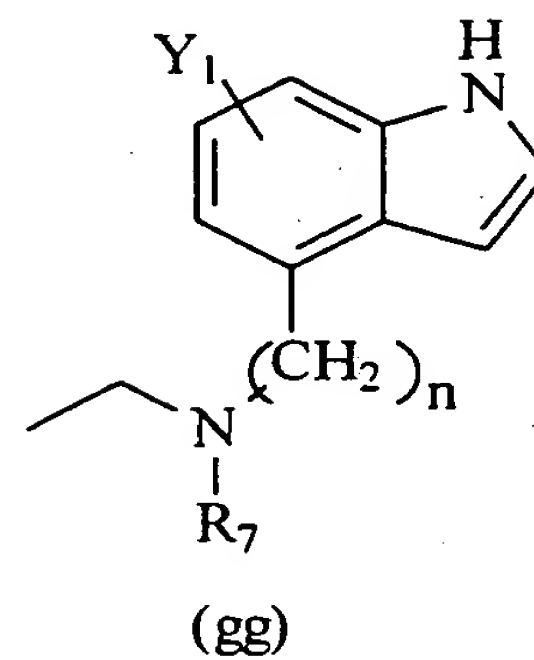
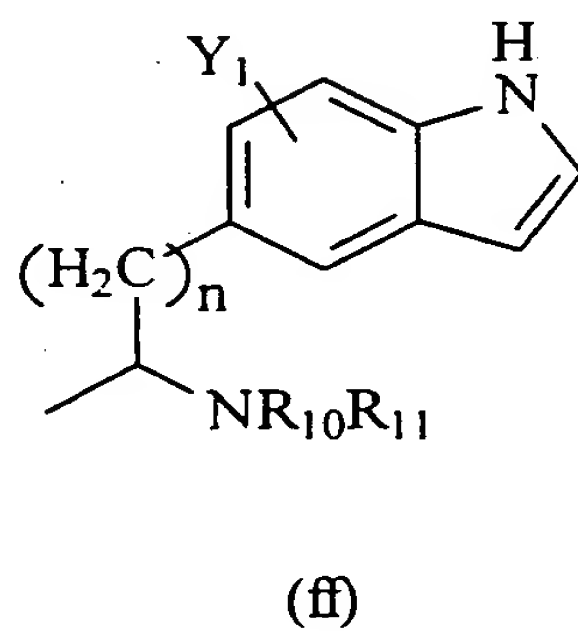
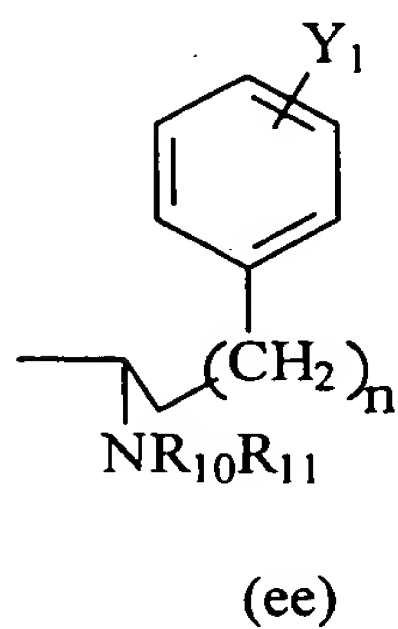
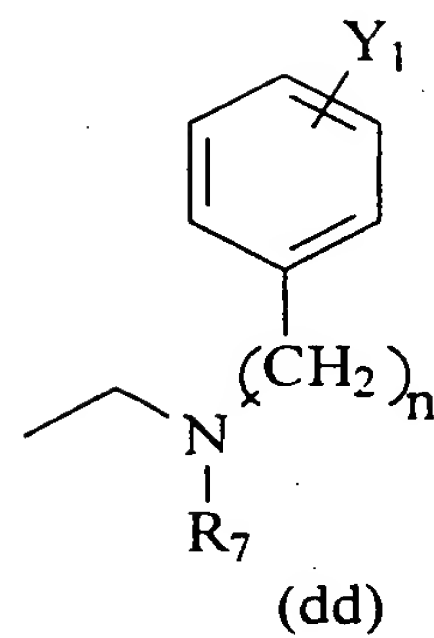
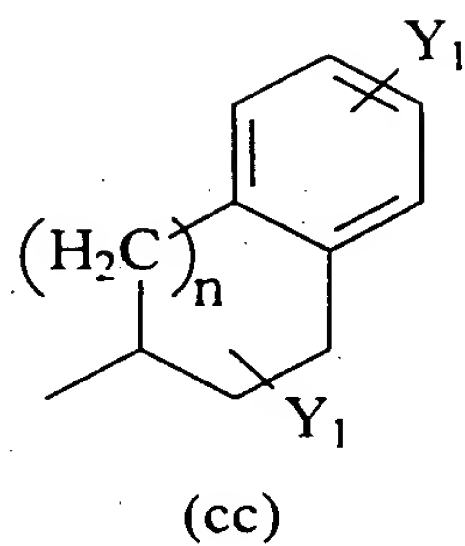
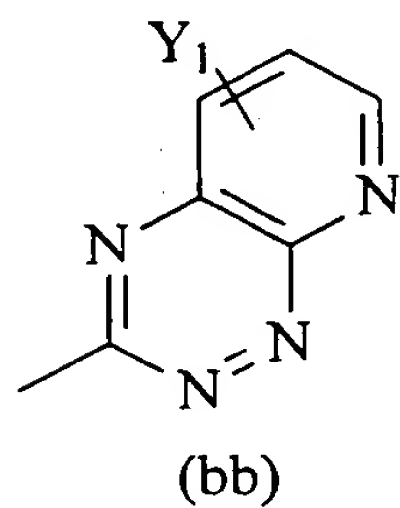
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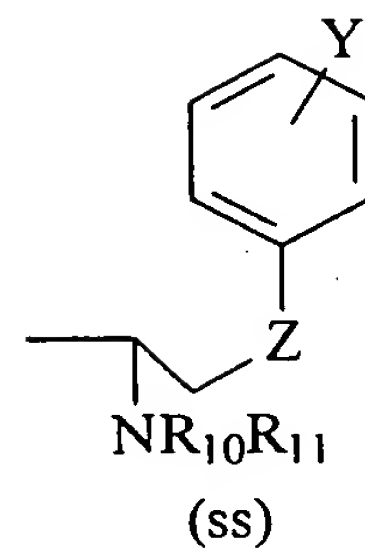
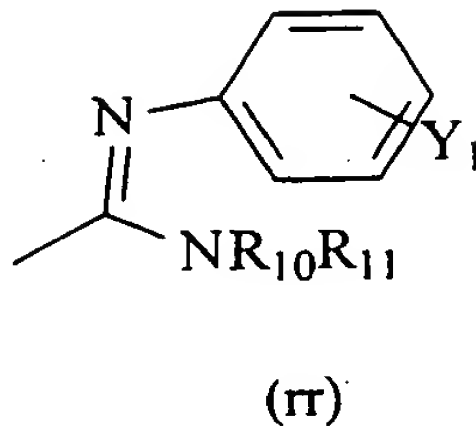
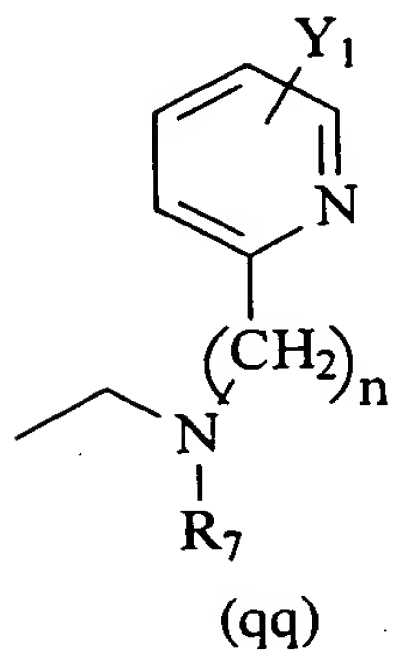
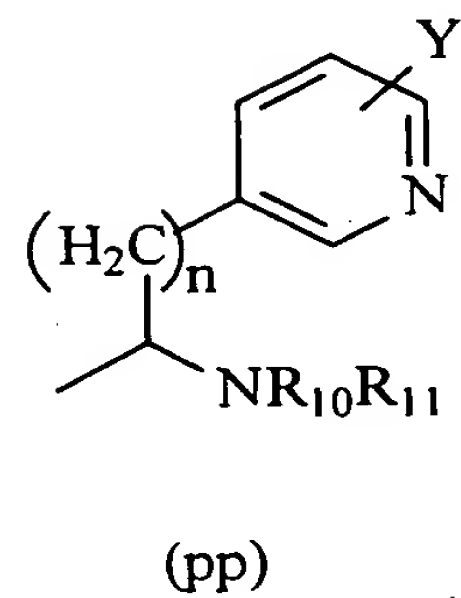
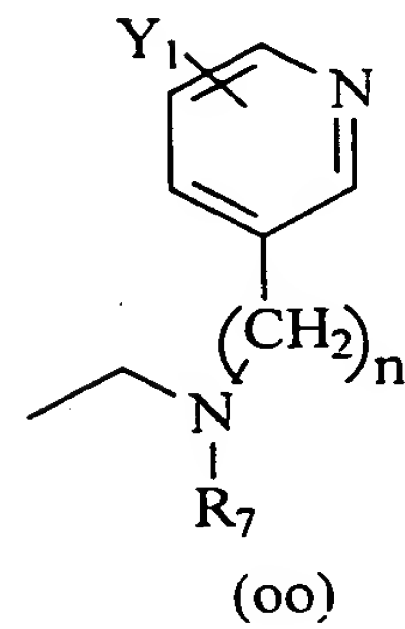
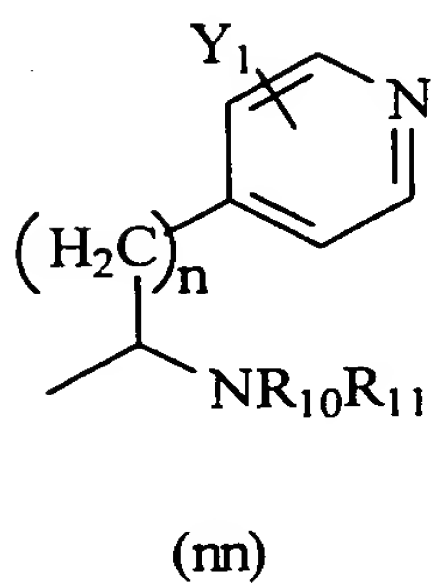
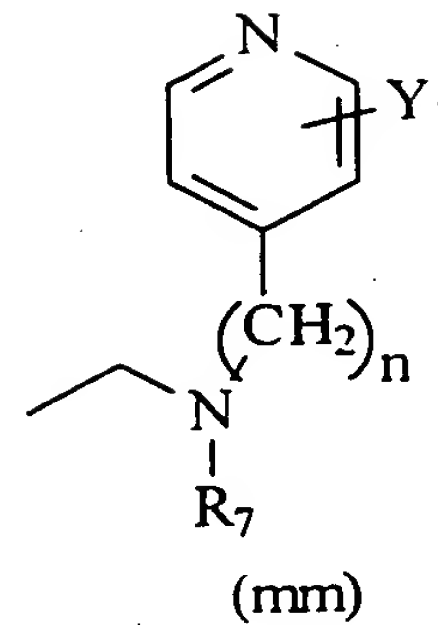
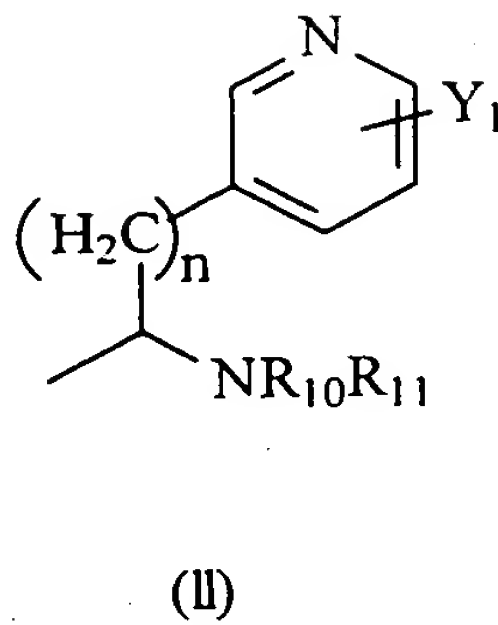
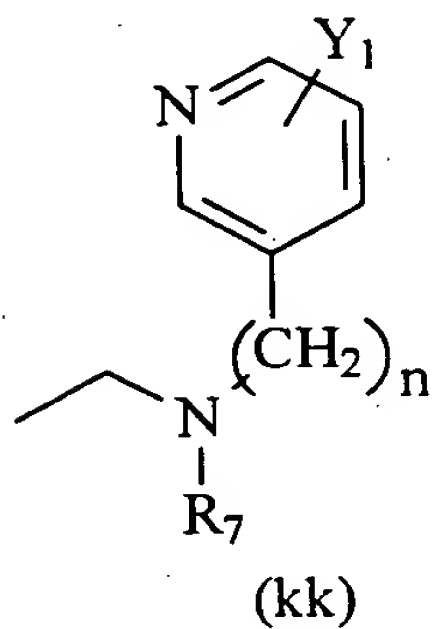


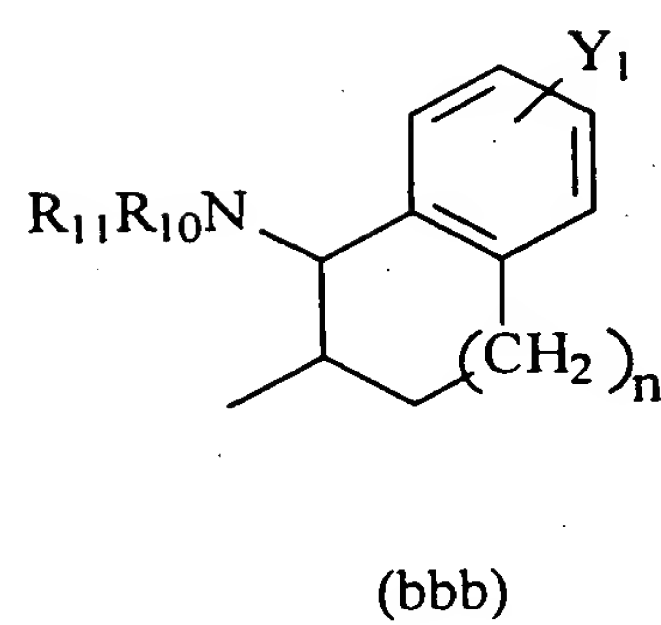
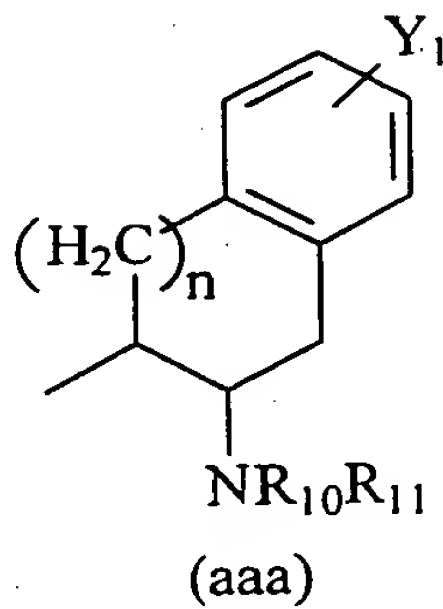
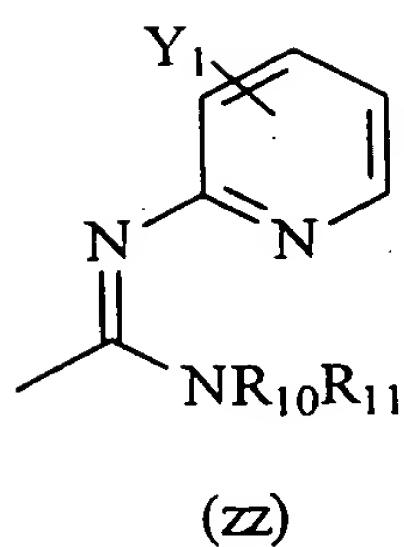
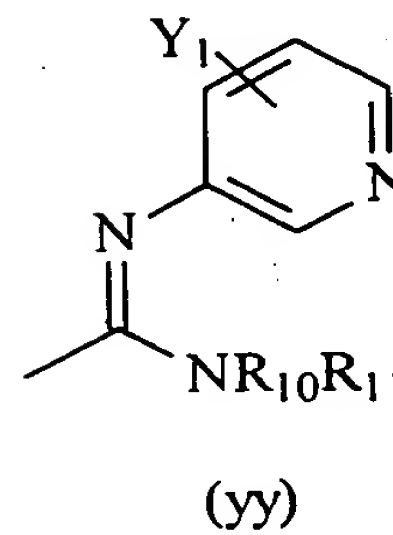
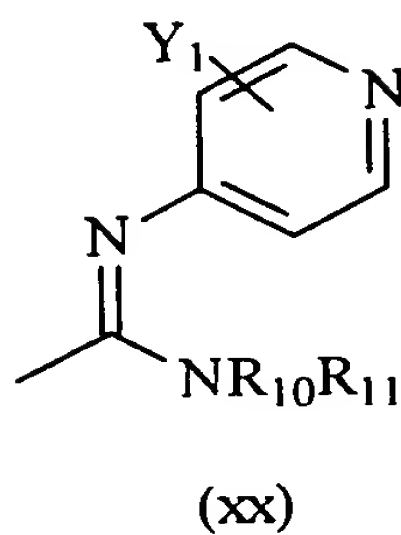
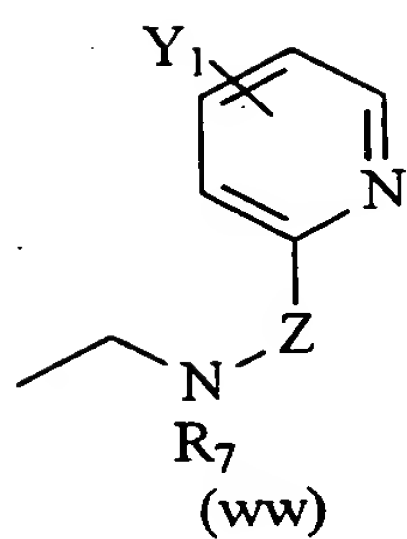
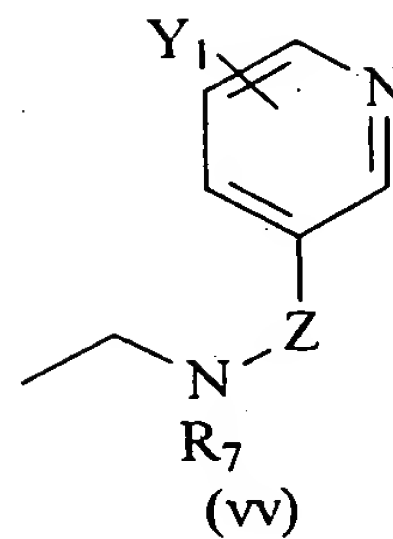
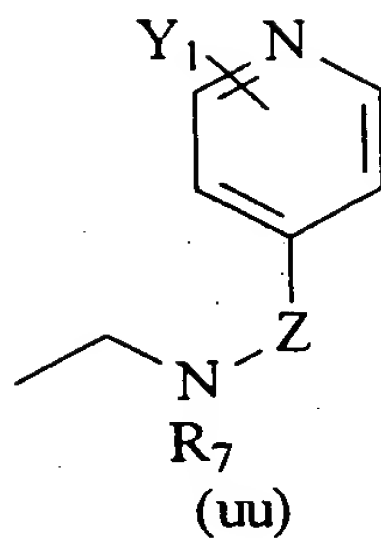
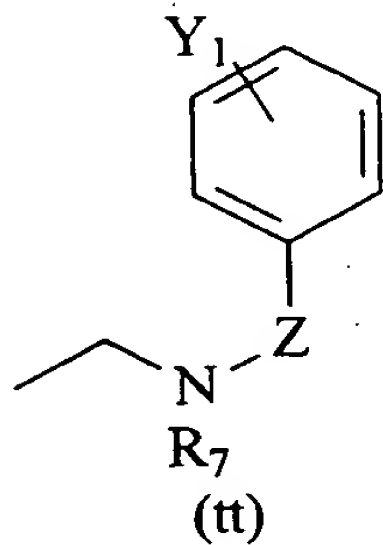
(i)













$X_1$  is hydrogen,  $C_{1-8}$  alkyl,  $C_{3-8}$  alkenyl, or  $C_{3-8}$  alkynyl;

$X_2$  is hydrogen,  $C_{1-8}$  alkyl,  $C_{3-8}$  alkenyl, or  $C_{3-8}$  alkynyl; or

$X_1$  and  $X_2$  together form  $=O$ ,  $=S$ ,  $=NH$ ;

$R_7$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_1$ ,  $NR_{10}$ ,  $R_{11}$ ,  $NHCOR_{12}$ ,  $NHCO_2R_{13}$ ,  $CONR_{14}R_{15}$ ,  $CH_2(CH_2)_nY_2$ , or  $C(=NH)NR_{16}R_{17}$ ;

$R_8$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_4$ ,  $CONR_{13}R_{14}$ , or  $CH_2(CH_2)_nY_2H$ ,  $OH$ ,  $Br$ ,  $Cl$ ,  $F$ ,  $CN$ ,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_9$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_5$ , or  $CH_2(CH_2)_nY_2H$ ,  $OH$ ,  $Br$ ,  $Cl$ ,  $F$ ,  $CN$ ,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_{10}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_6$ , or  $CH_2(CH_2)_nY_2H$ ,  $OH$ ,  $Br$ ,  $Cl$ ,  $F$ ,  $CN$ ,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_{11}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_7$ , or  $CH_2(CH_2)_nY_2H$ ,  $OH$ ,  $Br$ ,  $Cl$ ,  $F$ ,  $CN$ ,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_{12}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_8$ , or  $CH_2(CH_2)_nY_2H$ ,  $OH$ ,  $Br$ ,  $Cl$ ,  $F$ ,  $CN$ ,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_{13}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_9$ , or  $CH_2(CH_2)_nY_2H$ ,  $OH$ ,  $Br$ ,  $Cl$ ,  $F$ ,  $CN$ ,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_{14}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_4$ , or  $CH_2(CH_2)_nY_2$ , H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$ alkyl;

$R_{15}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_4$ , or  $CH_2(CH_2)_nY_2$ , H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$ alkyl;

$R_{16}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_4$ , or  $CH_2(CH_2)_nY_2$ , H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$ alkyl; and

$R_{17}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_4$ , or  $CH_2(CH_2)_nY_2$ , H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$ alkyl;

and pharmaceutically acceptable salts thereof.

Claim 2 (Previously Presented): The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein  $R_1$ ,  $R_4$ ,  $R_5$ ,  $Y_1$ ,  $Y_2$ ,  $Z$ ,  $n$ ,  $X_1$ ,  $X_2$ , and  $R_7$ - $R_{17}$  are as in Claim 1;

$Y_3$  is H;

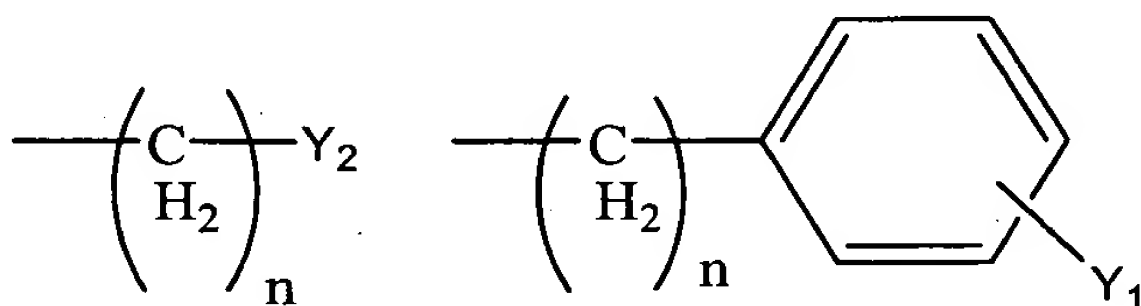
$R_2$  and  $R_3$  are each, independently, H,  $C_{1-8}$  alkyl,  $C_{3-8}$  alkynyl,  $C_{3-8}$  alkynyl, or  $CH_2$ aryl substituted by one or more substituents  $Y_1$ ; and

$R_6$  is a group having a formula selected from the group consisting of structures (a)-(cc);

and pharmaceutically acceptable salts thereof.

3. (Previously Presented) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I) wherein  $Y_1$ ,  $Y_2$ ,  $R_4$ ,  $R_5$ ,  $Z$ ,  $n$ ,  $X_1$ ,  $X_2$  and  $R_8$ - $R_{15}$  are as in Claim 1;

$R_1$  is  $C_{1-8}$  alkyl, or one of the following structures:



$Y_3$  is H;

$R_2$  and  $R_3$  are each, independently, H or  $C_{1-8}$  alkyl, wherein  $R_2$  and  $R_3$  cannot both be H at the same time;

$R_6$  is a formula selected from the structures (a)-(r); and

$R_7$  is H,  $C_{1-8}$  alkyl,  $CH_2$ aryl substituted by one or more substituents  $Y_1$ ,  $NR_{10}R_{11}$ ,  $NHCOR_{12}$ ,  $NHCO_2R_{13}$ ,  $CONR_{14}R_{15}$ , or  $CH_2(CH_2)_nY_2$ .

Claim 4 (Previously Presented) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I) wherein  $Y_1$ ,  $Z$ ,  $n$ ,  $X_1$ ,  $X_2$  and  $R_8$ - $R_{15}$  are as in Claim 1;

$R_1$  is  $C_{1-8}$  alkyl;

$Y_2$  is H,  $CF_3$ ,  $CO_2R_9$ ,  $C_{1-6}$  alkyl,  $NR_{10}R_{11}$ ,  $NHCOR_{12}$ ,  $NHCO_2R_{12}$ ,  $CONR_{13}R_{14}$ ,  $CH_2OH$ ,  $CH_2OR_8$ , or  $COCH_2R_9$ ;

$Y_3$  is H;

$R_2$  and  $R_3$  are each, independently, H or methyl, wherein  $R_2$  and  $R_3$  cannot both be H at the same time;

$R_4$  is H,  $C_{1-8}$  alkyl,  $CO_2C_{1-8}$ alkyl, or  $CH_2$  aryl substituted by one or more substituents  $Y_1$  and the stereocenter adjacent to  $R_4$  is in an (S) configuration;

$R_5$  is H,  $C_{1-8}$  alkyl, or  $CH_2CO_2C_{1-8}$  alkyl;

$R_6$  is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

$R_7$  is H,  $C_{1-8}$ alkyl,  $CH_2$ aryl substituted by one or more substituents  $Y_1$ ,  $NR_{10}R_{11}$ ,  $NHCO_2R_{12}$ ,  $NHCO_2R_{13}$ ,  $CONR_{14}R_{15}$ , or  $CH_2(CH_2)_nY_2$ .

Claim 5 (Previously Presented) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein  $Y_1$ , Z, n,  $X_1$ ,  $X_2$  and  $R_8$ - $R_{14}$  are as in Claim 1;

$R_1$  is methyl,

$Y_2$  is H,  $CF_3$ ,  $CO_2R_9$ ,  $C_{1-6}$  alkyl,  $NR_{10}R_{11}$ ,  $NHCO_2R_{12}$ ,  $NHCO_2R_{12}$ ,  $CONR_{13}R_{14}$ ,  $CH_2OH$ ,  $CH_2OR_8$ , or  $COCH_2R_9$ ;

$Y_3$  is H;

$R_2$  and  $R_3$  are each H or methyl, such that when  $R_2$  is H,  $R_3$  is methyl and vice versa;

$R_4$  is  $C_{1-8}$  alkyl, or  $CO_2C_{1-8}$  alkyl, and the stereocenter adjacent to  $R_4$  has a configuration of (S);

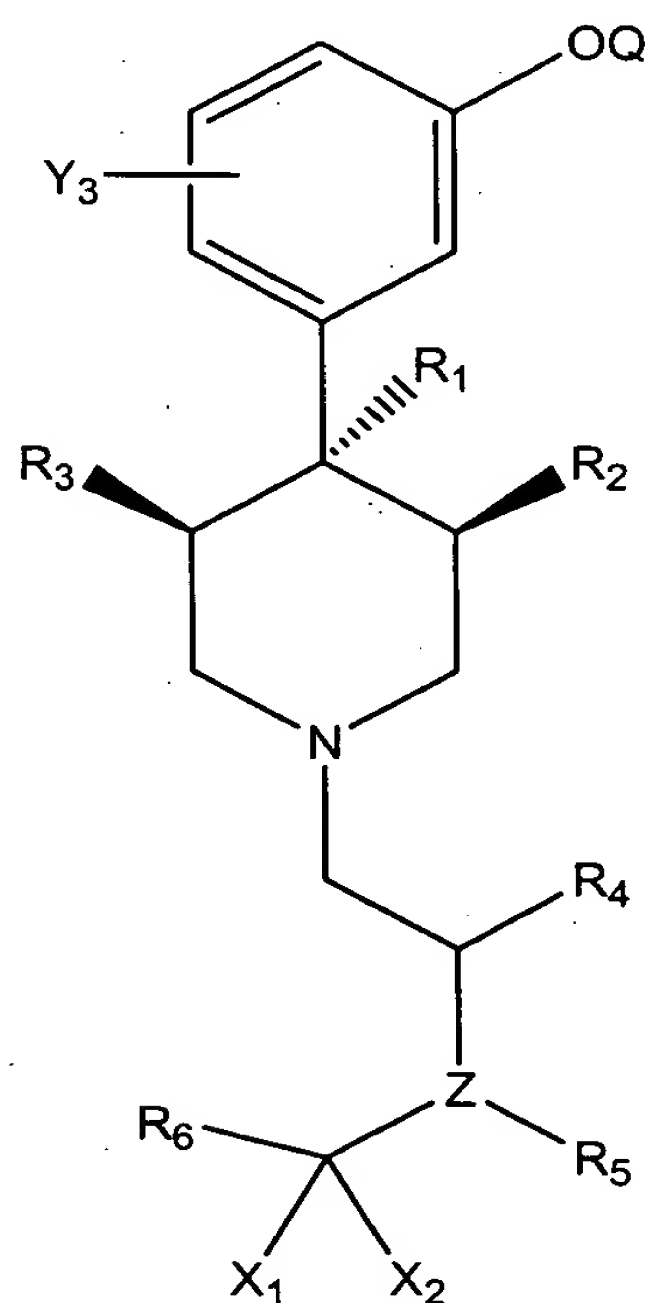
$R_5$  is H;

$R_6$  is a group having a formula selected from the group consisting of structures (a) and (b); and

$R_7$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_1$ , or  $CH_2(CH_2)_nY_2$ .

Claim 6 (Original) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound selected from formulae 14-21 of Fig. 1.

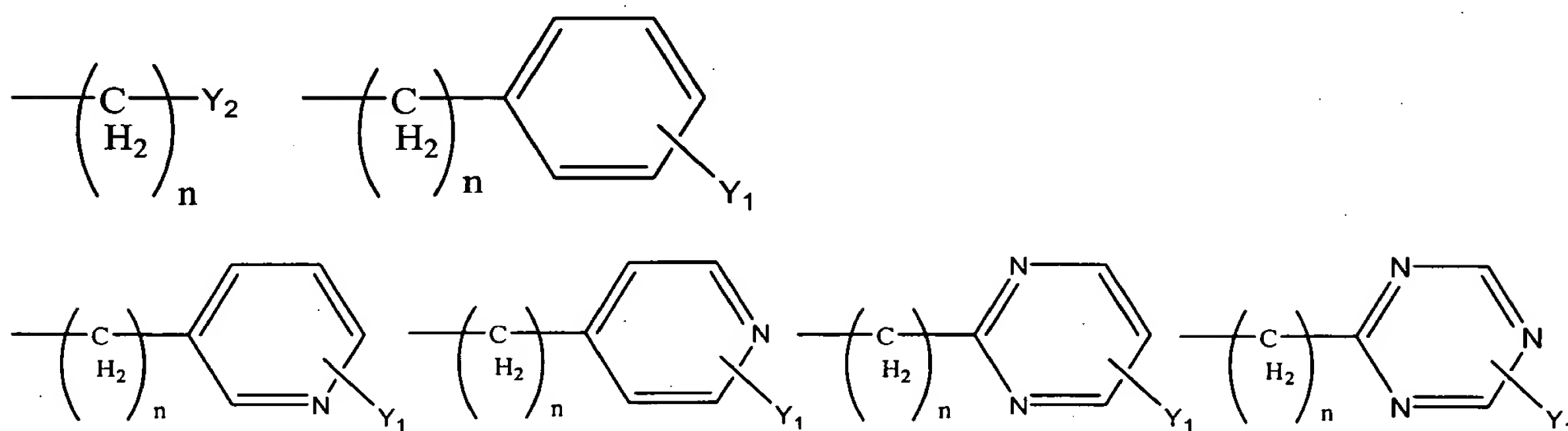
Claim 7 (Currently Amended) A kappa opioid receptor antagonist compound  
 represented by the formula (I):



(I)

wherein Q is H or COC<sub>1-8</sub> alkyl;

R<sub>1</sub> is C<sub>1-8</sub> alkyl, or one of the following structures:



Y<sub>1</sub> is H, OH, Br, Cl, F, CN, CF<sub>3</sub>, NO<sub>2</sub>, N<sub>3</sub>, OR<sub>8</sub>, CO<sub>2</sub>R<sub>9</sub>, C<sub>1-6</sub> alkyl, NR<sub>10</sub>R<sub>11</sub>,

NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>12</sub>, CONR<sub>13</sub>R<sub>14</sub>, or CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>;

$Y_2$  is H,  $CF_3$ ,  $CO_2R_9$ ,  $C_{1-6}$ alkyl,  $NR_{10}R_{11}$ ,  $NHCOR_{12}$ ,  $NHCO_2R_{12}$ ,  $CONR_3R_{14}$ ,  $CH_2OH$ ,  $CH_2OR_8$ , or  $COCH_2R_9$ ;

$Y_3$  is H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $OR_8$ ,  $CO_2R_9$ ,  $C_{1-6}$  alkyl,  $NR_{10}R_{11}$ ,  $NHCOR_{12}$ ,  $NHCO_2R_{12}$ ,  $CONR_{13}R_{14}$ , or  $CH_2(CH_2)_n Y_2$ ;

$R_2$  is H,  $C_{1-8}$  alkyl,  $C_{3-8}$ alkenyl,  $C_{3-8}$  alkynyl or  $CH_2$ aryl substituted by one or more groups  $Y_1$ ;

$R_3$  is H,  $C_{1-8}$  alkyl,  $C_{3-8}$  alkenyl,  $C_{3-8}$  alkynyl or  $CH_2$ aryl substituted by one or more groups  $Y_1$ ;

wherein  $R_2$  and  $R_3$  may be bonded together to form a  $C_{2-8}$  alkyl group;

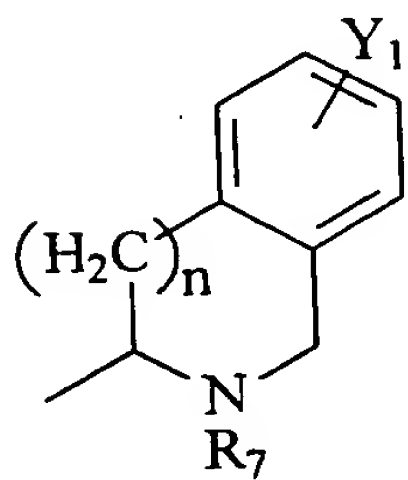
$R_4$  is hydrogen,  $C_{1-8}$  alkyl,  $CO_2C_{1-8}$  alkylaryl substituted by one or more groups  $Y_1$ ,  $CH_2$ aryl substituted by one or more groups  $Y_1$  or  $CO_2C_{1-8}$  alkyl;

$Z$  is N, O or S; when  $Z$  is O or S there is no  $R_5$

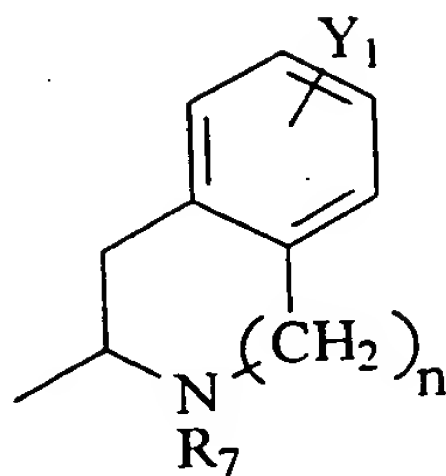
$R_5$  is H,  $C_{1-8}$  alkyl,  $C_{3-8}$  alkenyl,  $C_{3-8}$  alkynyl,  $CH_2CO_2C_{1-8}$  alkyl,  $CO_2C_{1-8}$  alkyl or  $CH_2$ aryl substituted by one or more groups  $Y_1$ ;

$n$  is 0, 1, 2 or 3;

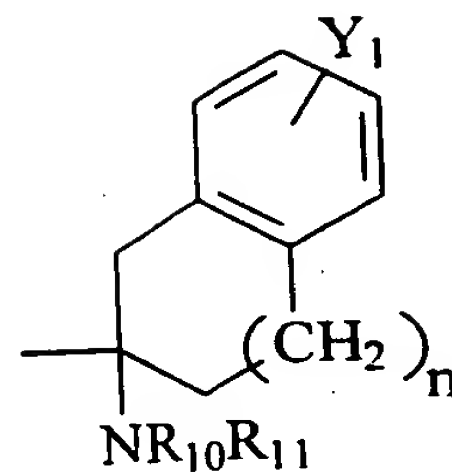
$R_6$  is a group selected from the group consisting of structures (a)-(bbb):



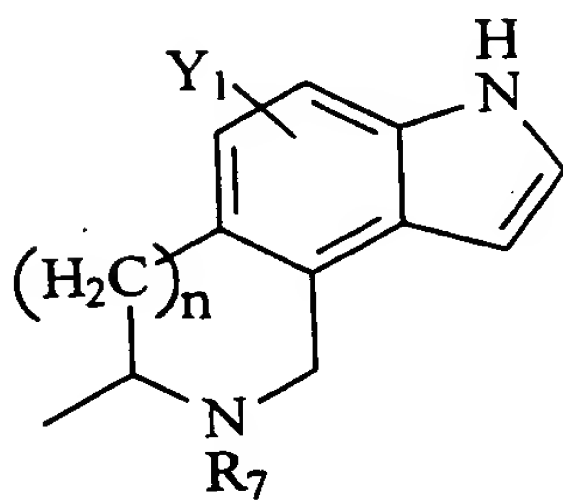
(a)



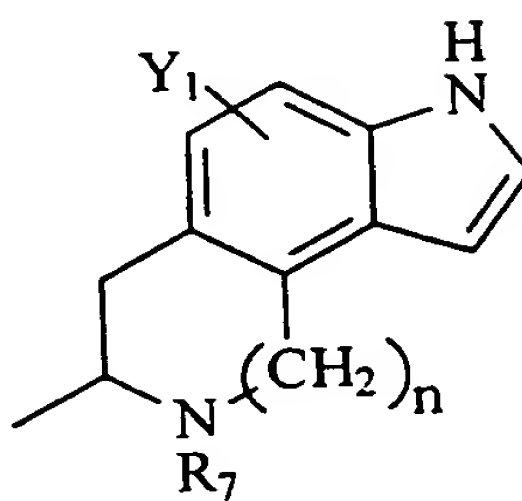
(b)



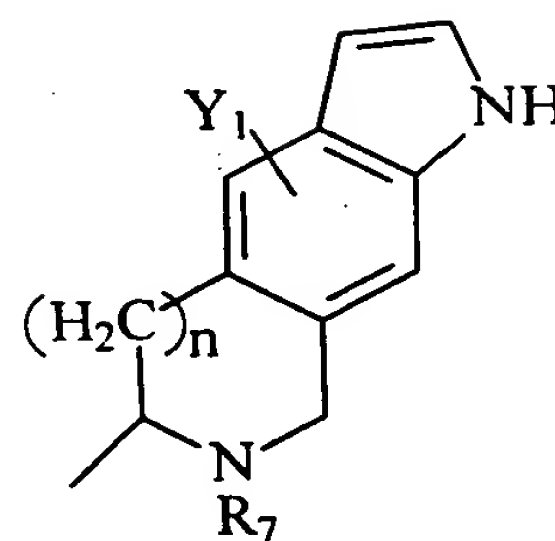
(c)



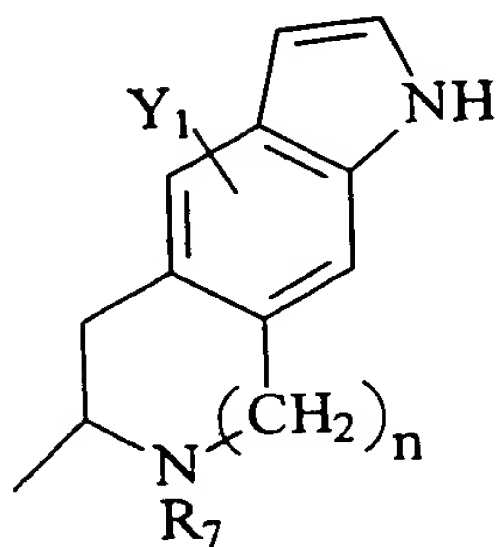
(d)



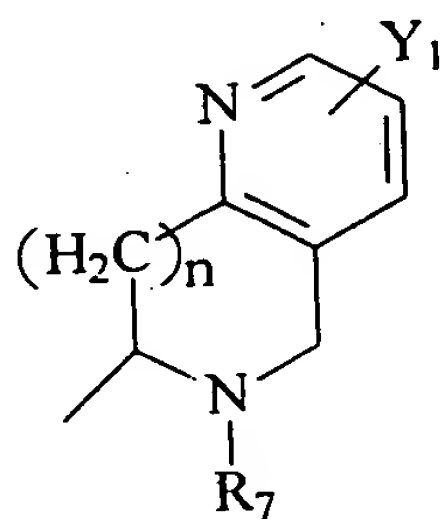
(e)



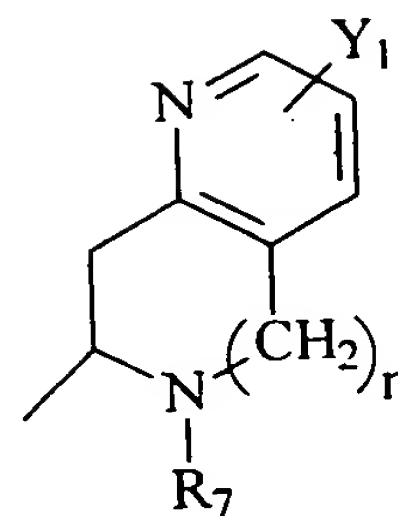
(f)



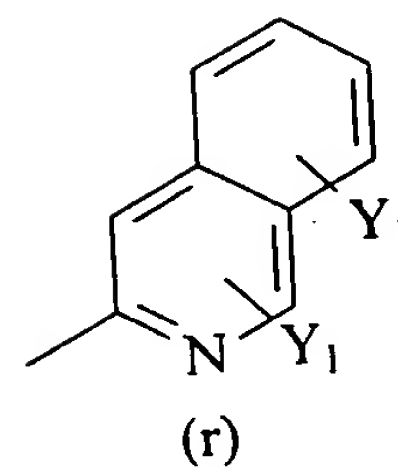
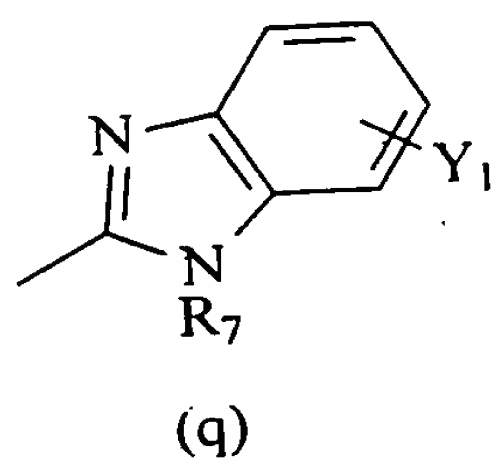
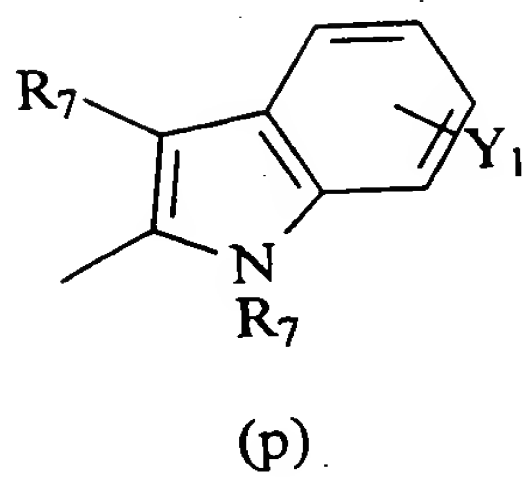
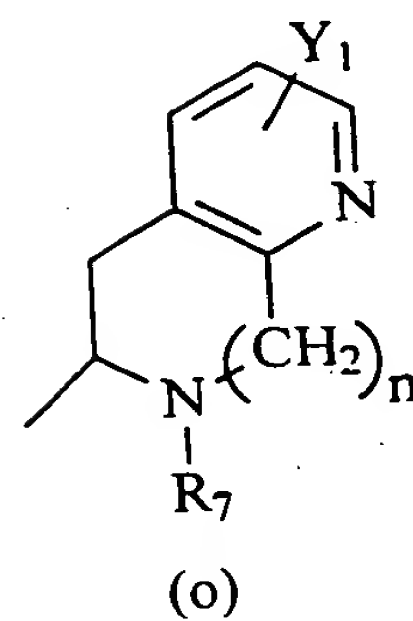
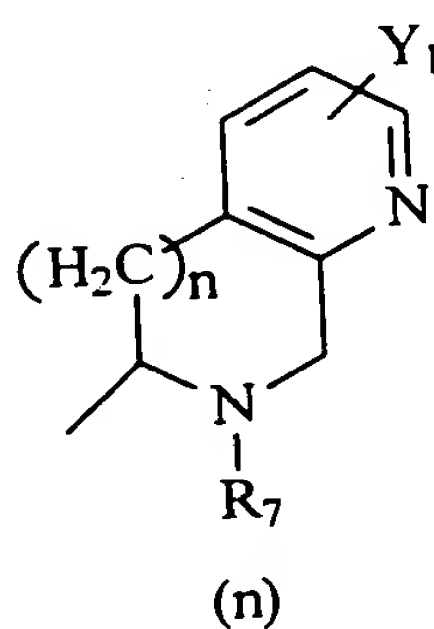
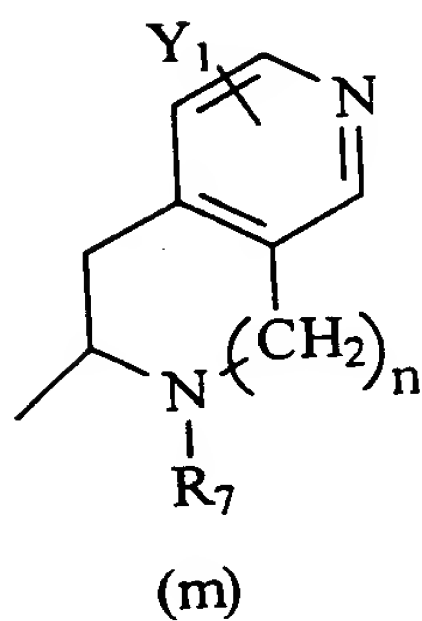
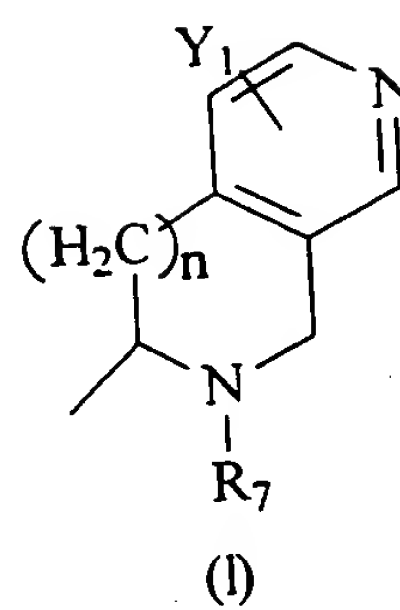
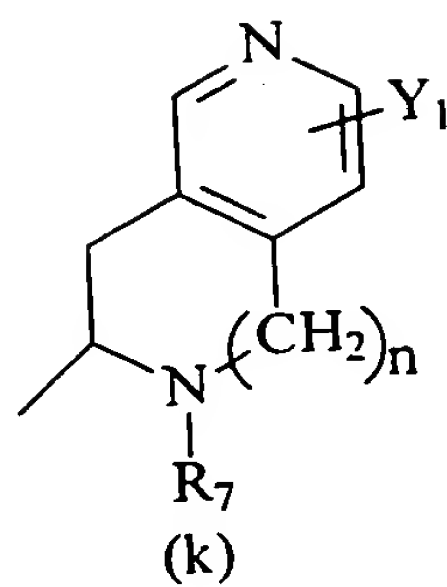
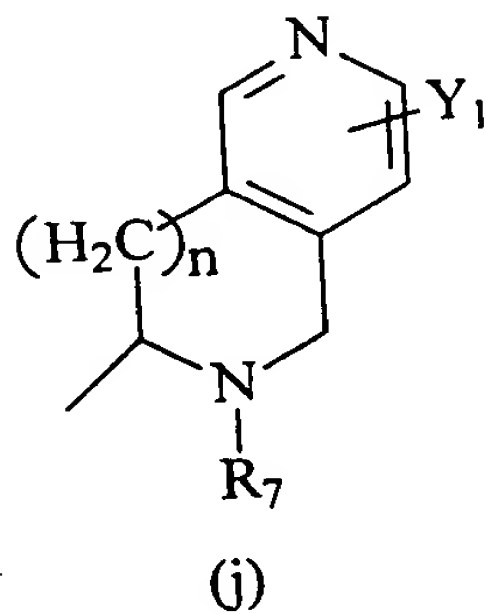
(g)



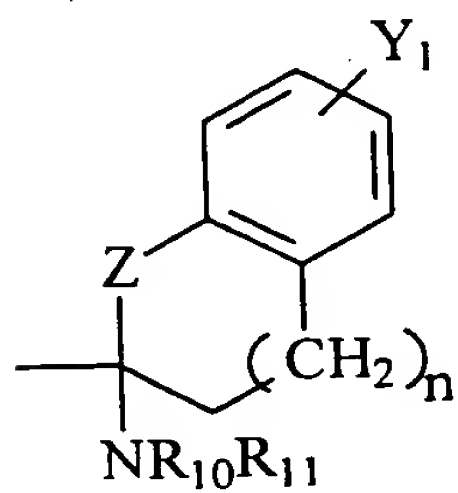
(h)



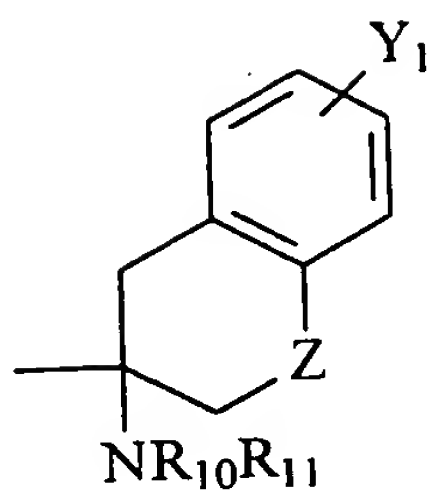
(i)



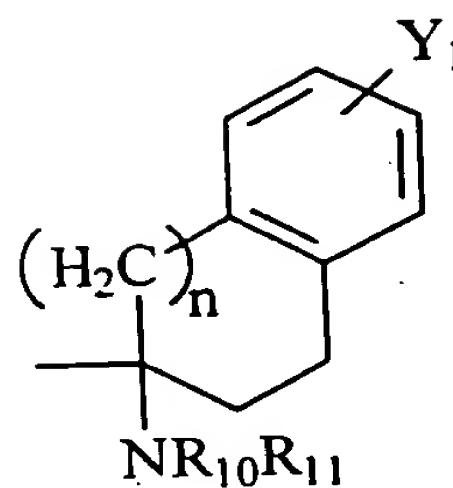




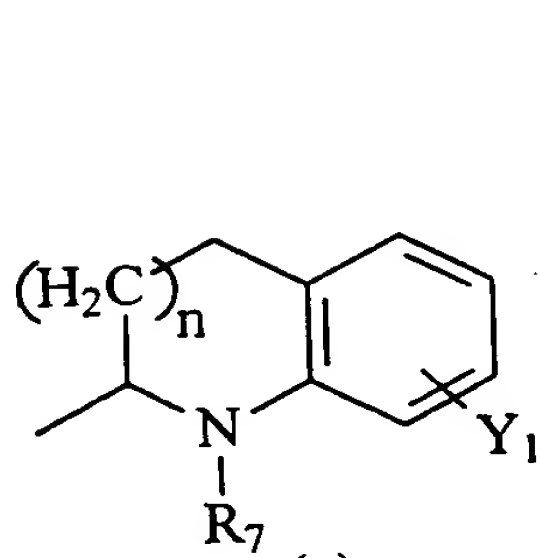
(s)



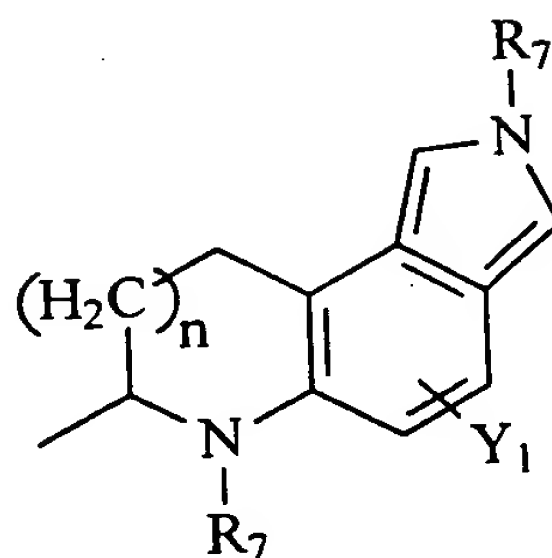
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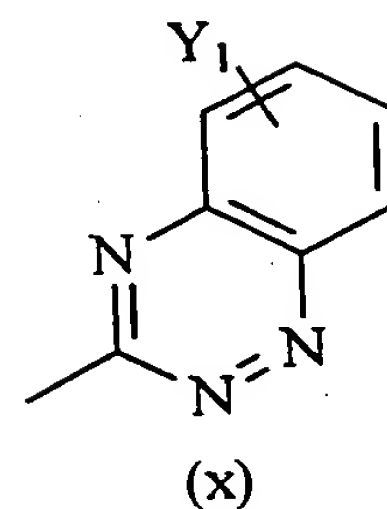
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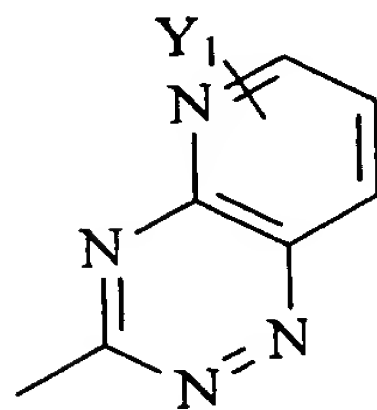
(v)



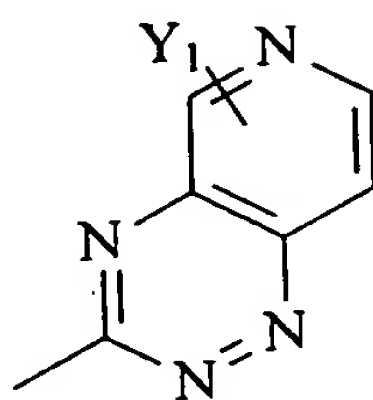
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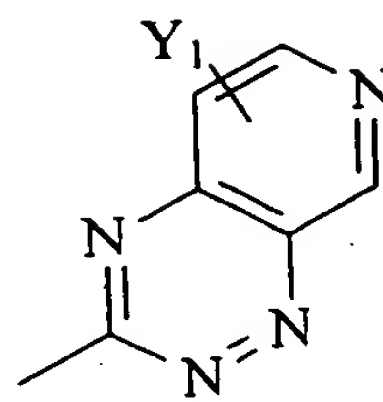
(x)



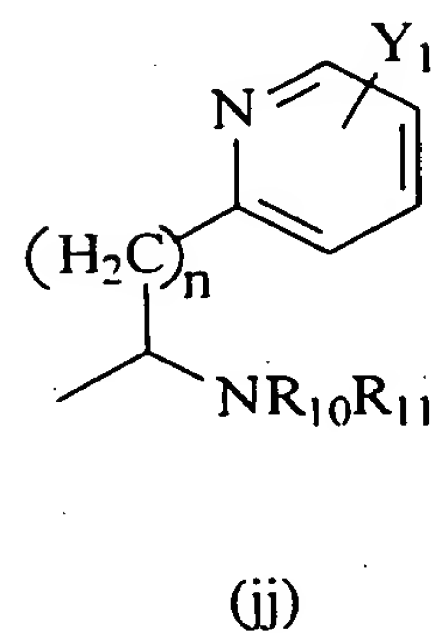
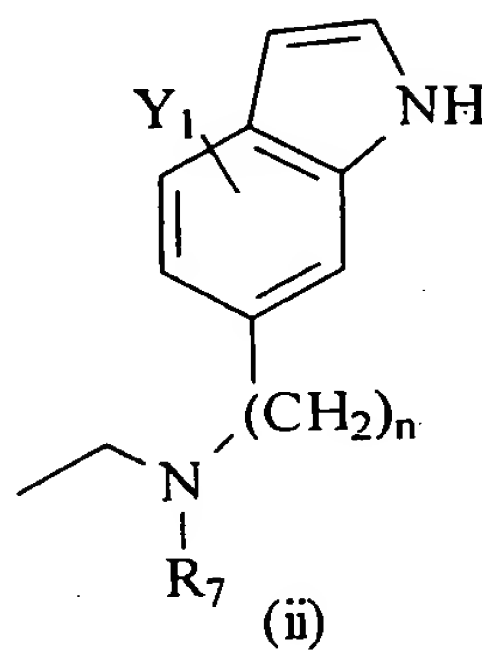
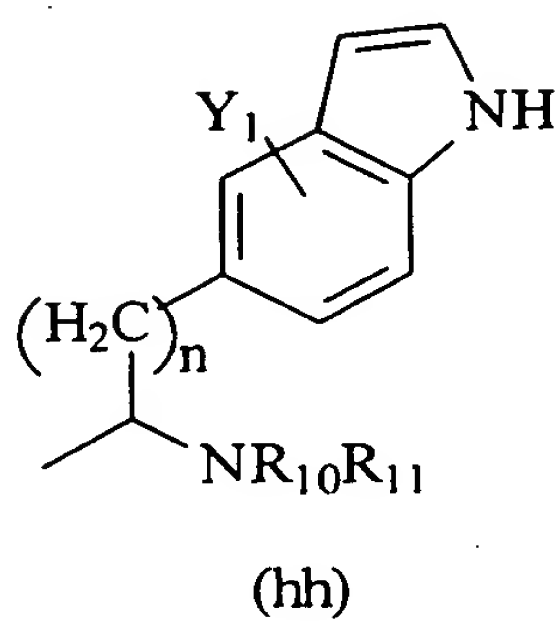
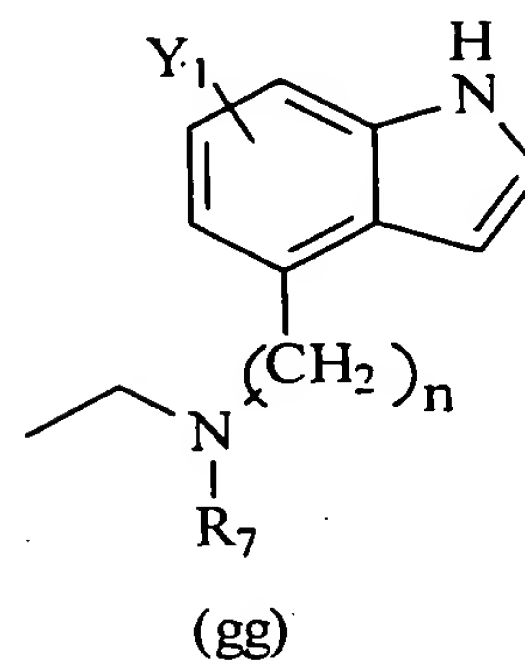
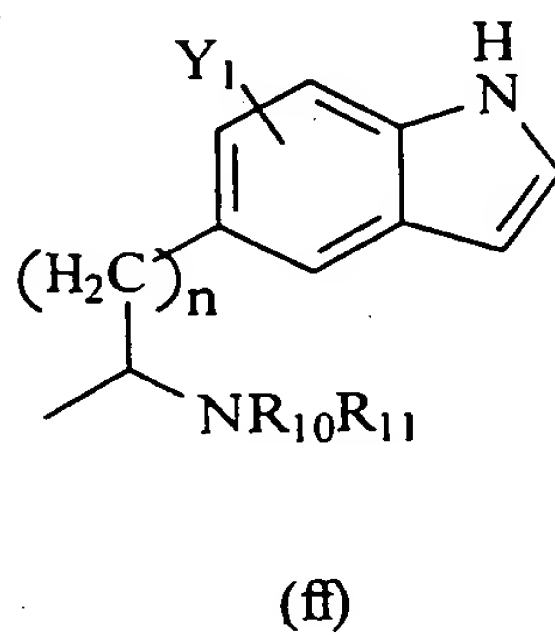
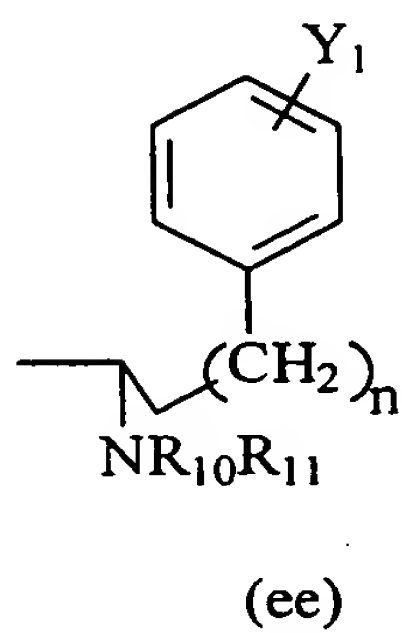
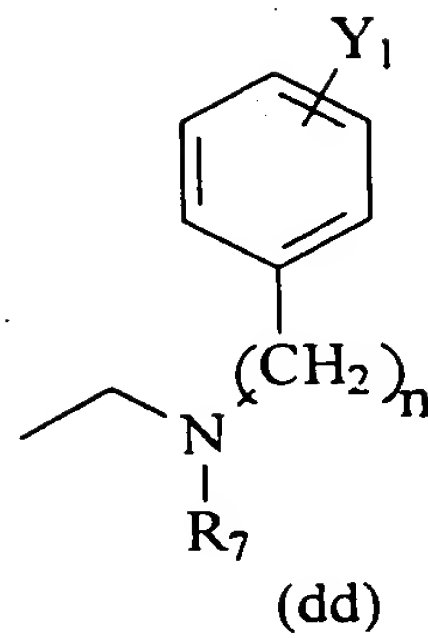
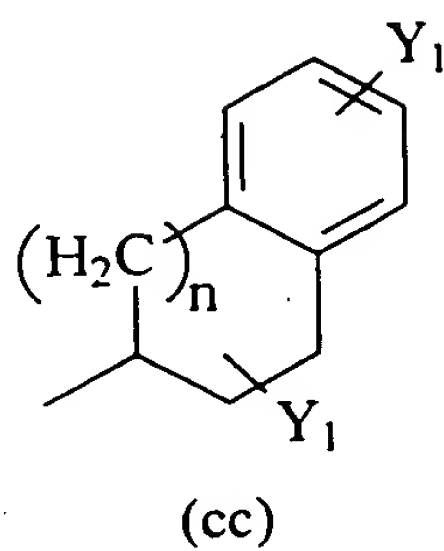
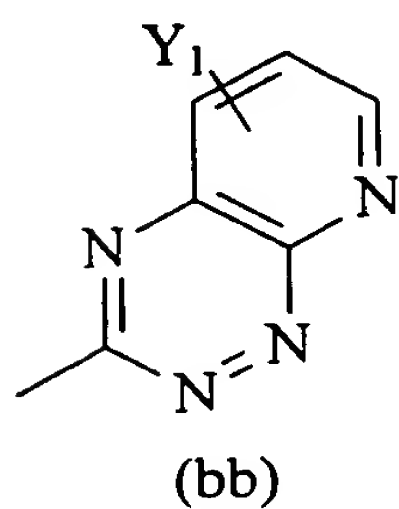
(y)

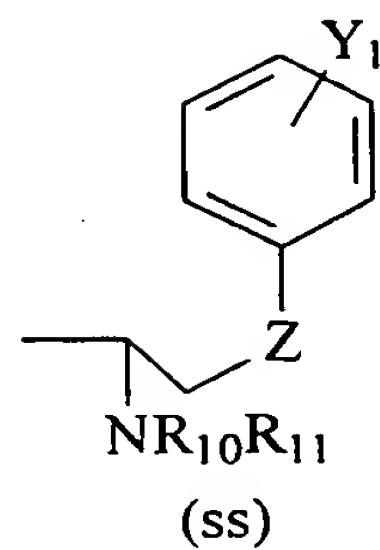
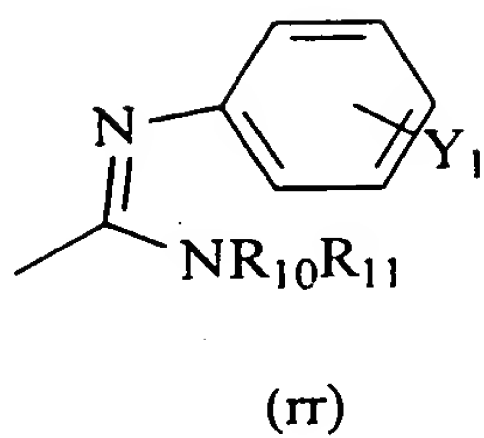
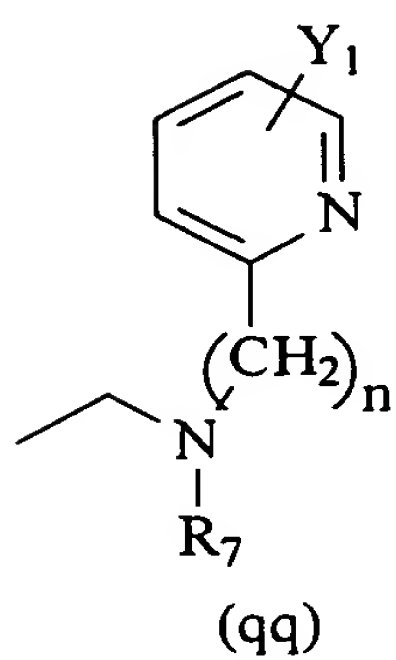
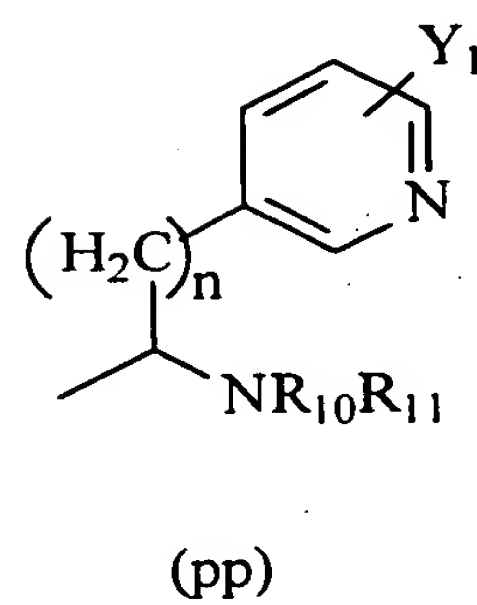
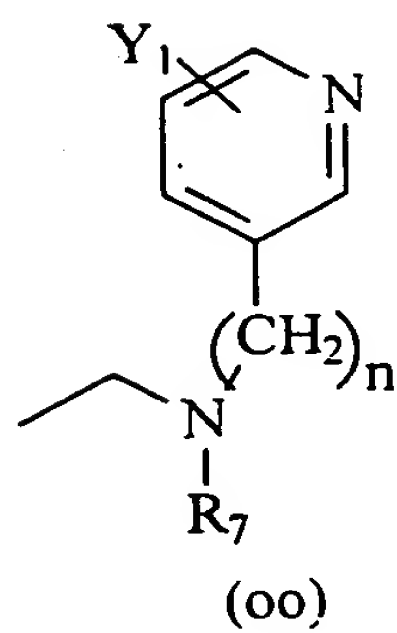
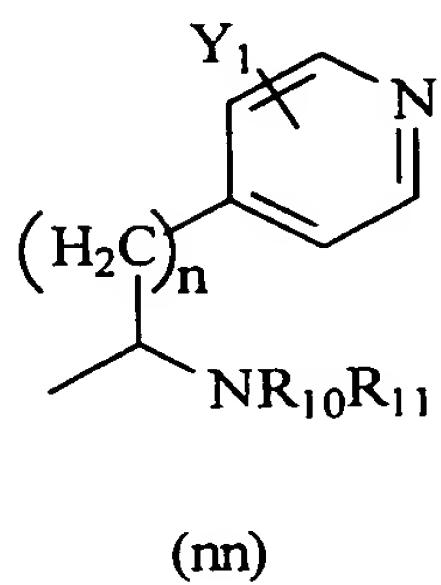
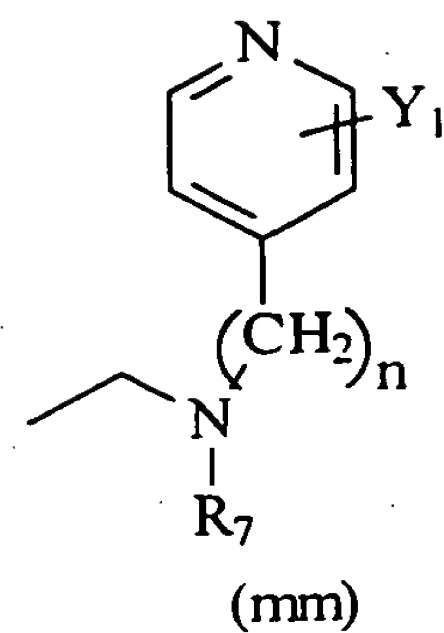
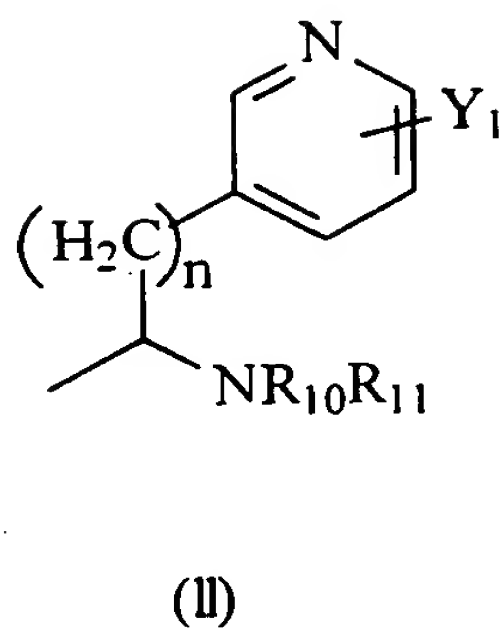
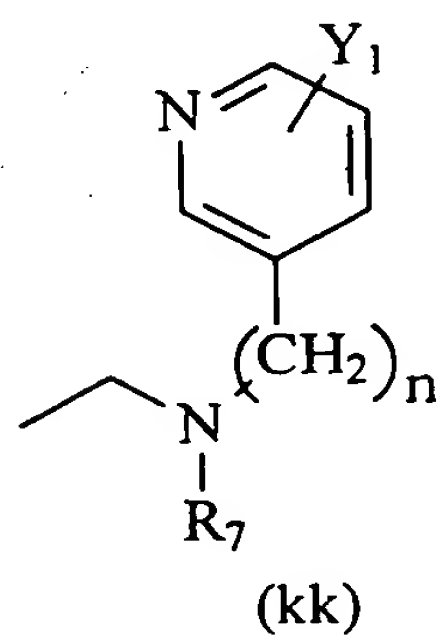


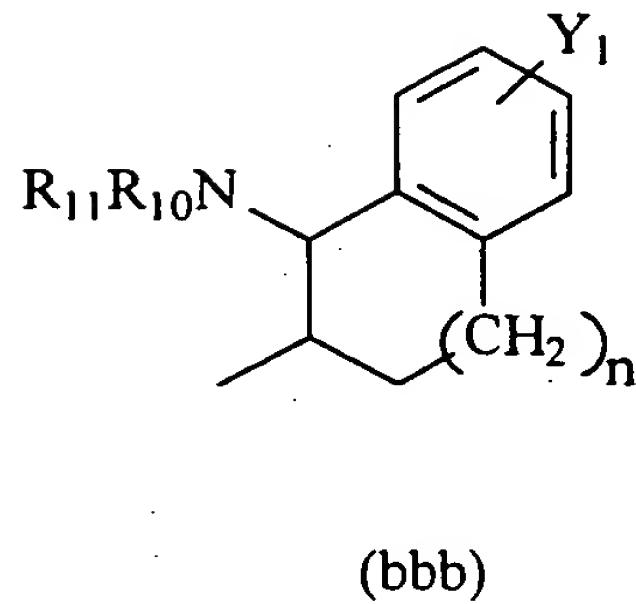
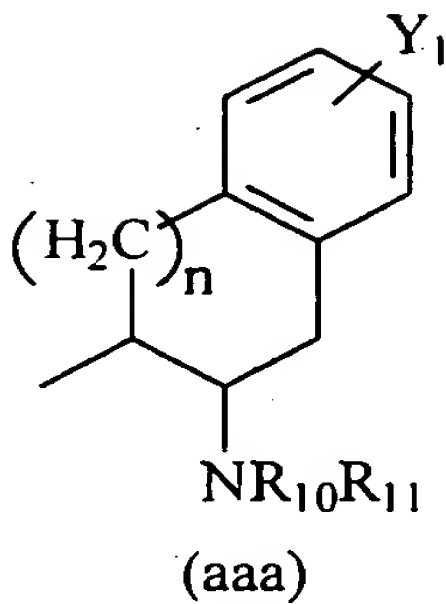
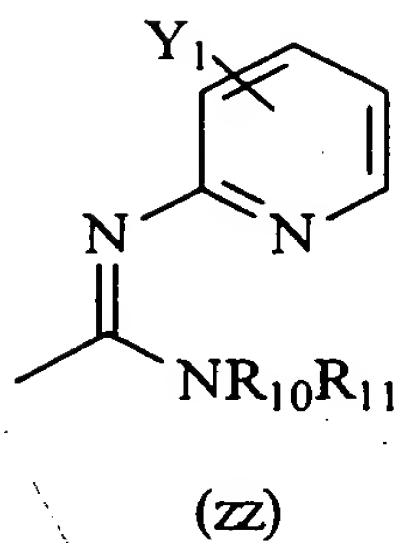
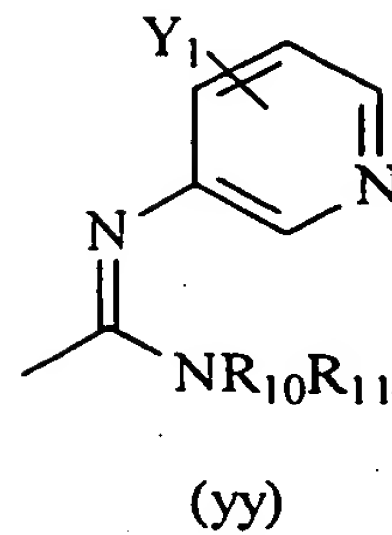
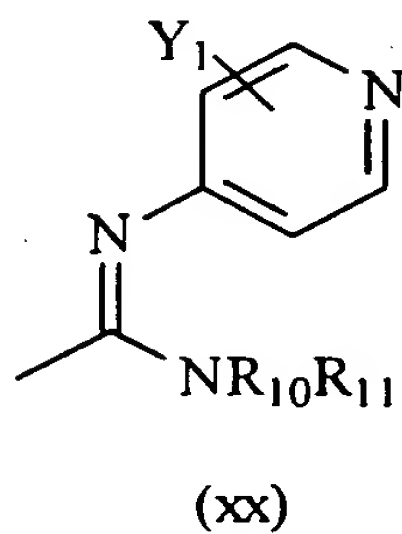
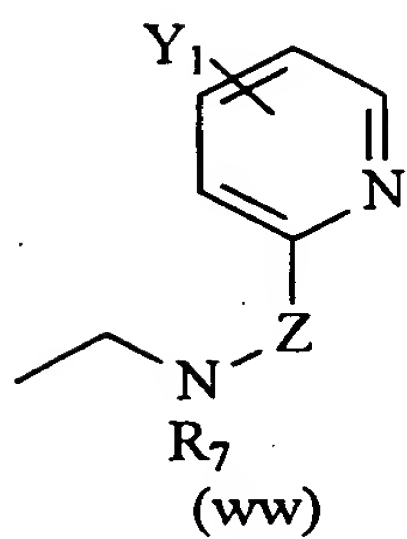
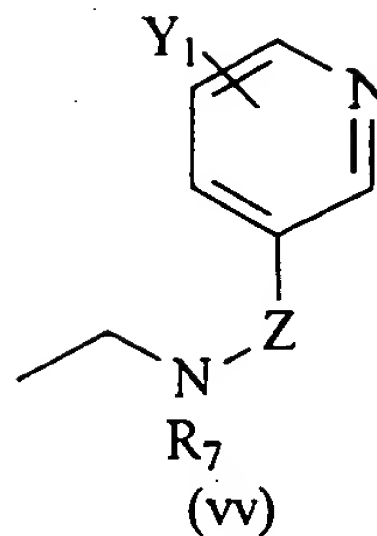
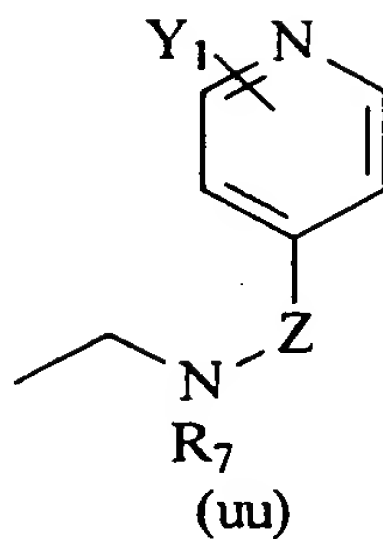
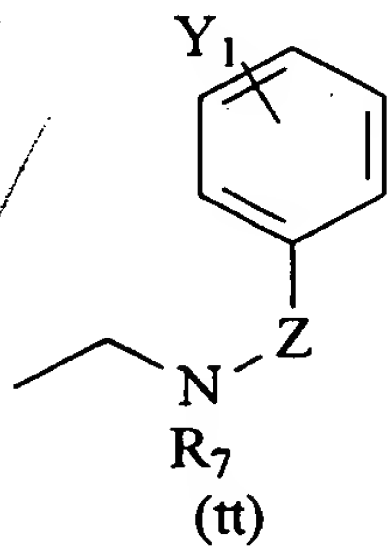
(z)



(aa)







$X_1$  is hydrogen,  $C_{1-8}$  alkyl,  $C_{3-8}$  alkenyl, or  $C_{3-8}$  alkynyl;

$X_2$  is hydrogen,  $C_{1-8}$  alkyl,  $C_{3-8}$  alkenyl, or  $C_{3-8}$  alkynyl;

or  $X_1$  and  $X_2$  together form  $=O$ ,  $=S$ , or  $=NH$ ;

$R_7$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_1$ ,  $NR_{10}R_{11}$ ,  $NHCOR_{12}$ ,  $NHCO_2R_{13}$ ,  $CONR_{14}R_{15}$ ,  $CH_2(CH_2)_nY_2$ , or  $C(=NH)NR_{16}R_{17}$ ;

$R_8$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_4$ ,  $CONR_{13}R_{14}$ , or  $CH_2(CH_2)_nY_2H$ , OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_9$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_4$ , or  $CH_2(CH_2)_nY_2H$ , OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_{10}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_4$ , or  $CH_2(CH_2)_nY_2H$ , OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_{11}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_4$ , or  $CH_2(CH_2)_nY_2H$ , OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_{12}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_4$ , or  $CH_2(CH_2)_nY_2H$ , OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_{13}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_4$ , or  $CH_2(CH_2)_nY_2H$ , OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_{14}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_4$ , or  $CH_2(CH_2)_nY_2$  H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$ alkyl;

$R_{15}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_4$ , or  $CH_2(CH_2)_nY_2$  H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$ alkyl;

$R_{16}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_4$ , or  $CH_2(CH_2)_nY_2$  H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$ alkyl; and

$R_{17}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_4$ , or  $CH_2(CH_2)_nY_2$  H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$ alkyl

and pharmaceutically acceptable salts thereof.

Claim 8 (Previously Presented) The kappa opioid receptor antagonist compound of claim 7, wherein  $R_1$ ,  $R_4$ ,  $R_5$ ,  $Y_1$ ,  $Y_2$ ,  $Z$ ,  $n$ ,  $X_1$ ,  $X_2$ , and  $R_7$ - $R_{17}$  are as in Claim 7;

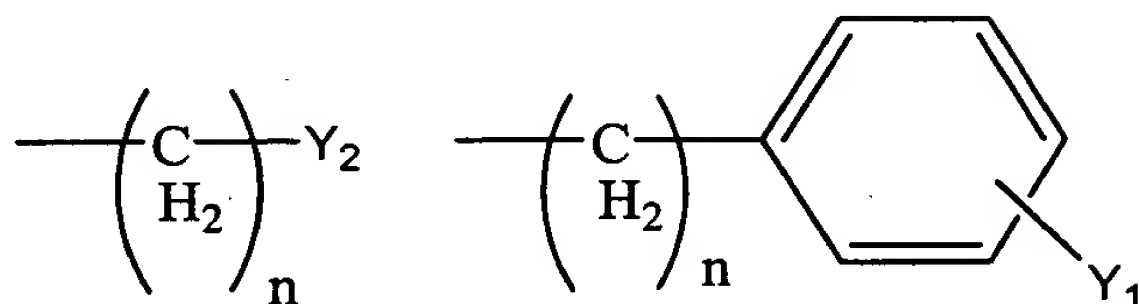
$Y_3$  is H;

$R_2$  and  $R_3$  are each, independently, H,  $C_{1-8}$  alkyl,  $C_{3-8}$  alkynyl,  $C_{3-8}$  alkynyl, or  $CH_2$ aryl substituted by one or more substituents  $Y_1$ ; and

$R_6$  is a group having a formula selected from the group consisting of structures (a)-(cc).

Claim 9 (Previously Presented) The kappa opioid receptor antagonist compound of claim 7, wherein  $Y_1$ ,  $Y_2$ ,  $R_4$ ,  $R_5$ ,  $Z$ ,  $n$ ,  $X_1$ ,  $X_2$  and  $R_8$ - $R_{15}$  are as in Claim 7;

$R_1$  is  $C_{1-8}$  alkyl, or one of the following structures:



$Y_3$  is H;

$R_2$  and  $R_3$  are each, independently, H or  $C_{1-8}$  alkyl, wherein  $R_2$  and  $R_3$  cannot both be H at the same time;

$R_6$  is a formula selected from the structures (a)-(r); and

$R_7$  is H,  $C_{1-8}$  alkyl,  $CH_2$ aryl substituted by one or more substituents  $Y_1$ ,  $NR_{10}R_{11}$ ,  $NHCOR_{12}$ ,  $NHCO_2R_{13}$ ,  $CONR_{14}R_{15}$ , or  $CH_2(CH_2)_nY_2$ .

Claim 10 (Previously Presented) The kappa opioid receptor antagonist compound of claim 7, wherein  $Y_1$ , Z, n,  $X_1$ ,  $X_2$  and  $R_8$ - $R_{15}$  are as in Claim 7;

$R_1$  is  $C_{1-8}$  alkyl;

$Y_2$  is H,  $CF_3$ ,  $CO_2R_9$ ,  $C_{1-6}$  alkyl,  $NR_{10}R_{11}$ ,  $NHCOR_{12}$ ,  $NHCO_2R_{12}$ ,  $CONR_{13}R_{14}$ ,  $CH_2OH$ ,  $CH_2OR_8$ , or  $COCH_2R_9$ ;

$Y_3$  is H;

$R_2$  and  $R_3$  are each, independently, H or methyl, wherein  $R_2$  and  $R_3$  cannot both be H at the same time;

$R_4$  is H,  $C_{1-8}$  alkyl,  $CO_2C_{1-8}$ alkyl, or  $CH_2$  aryl substituted by one or more substituents  $Y_1$  and the stereocenter adjacent to  $R_4$  is in an (S) configuration;

$R_5$  is H,  $C_{1-8}$  alkyl,  $CH_2CO_2C_{1-8}$  alkyl;

$R_6$  is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

$R_7$  is H,  $C_{1-8}$ alkyl,  $CH_2$ aryl substituted by one or more substituents  $Y_1$ ,  $NR_{10}R_{11}$ ,  $NHCOR_{12}$ ,  $NHCO_2R_{13}$ ,  $CONR_{14}R_{15}$ , or  $CH_2(CH_2)_nY_2$ .

Claim 11 (Previously Presented) The kappa opioid receptor antagonist compound of claim 7, wherein  $Y_1$ ,  $Z$ ,  $n$ ,  $X_1$ ,  $X_2$  and  $R_8$ - $R_{14}$  are as in Claim 7;

$R_1$  is methyl,

$Y_2$  is H,  $CF_3$ ,  $CO_2R_9$ ,  $C_{1-6}$  alkyl,  $NR_{10}R_{11}$ ,  $NHCOR_{12}$ ,  $NHCO_2R_{12}$ ,  $CONR_{13}R_{14}$ ,  $CH_2OH$ ,  $CH_2OR_8$ , or  $COCH_2R_9$ ;

$Y_3$  is H;

$R_2$  and  $R_3$  are each H or methyl, such that when  $R_2$  is H,  $R_3$  is methyl and vice versa;

$R_4$  is  $C_{1-8}$  alkyl, or  $CO_2C_{2-8}$  alkyl, and the stereocenter adjacent to  $R_4$  has a configuration of (S);

$R_5$  is H;

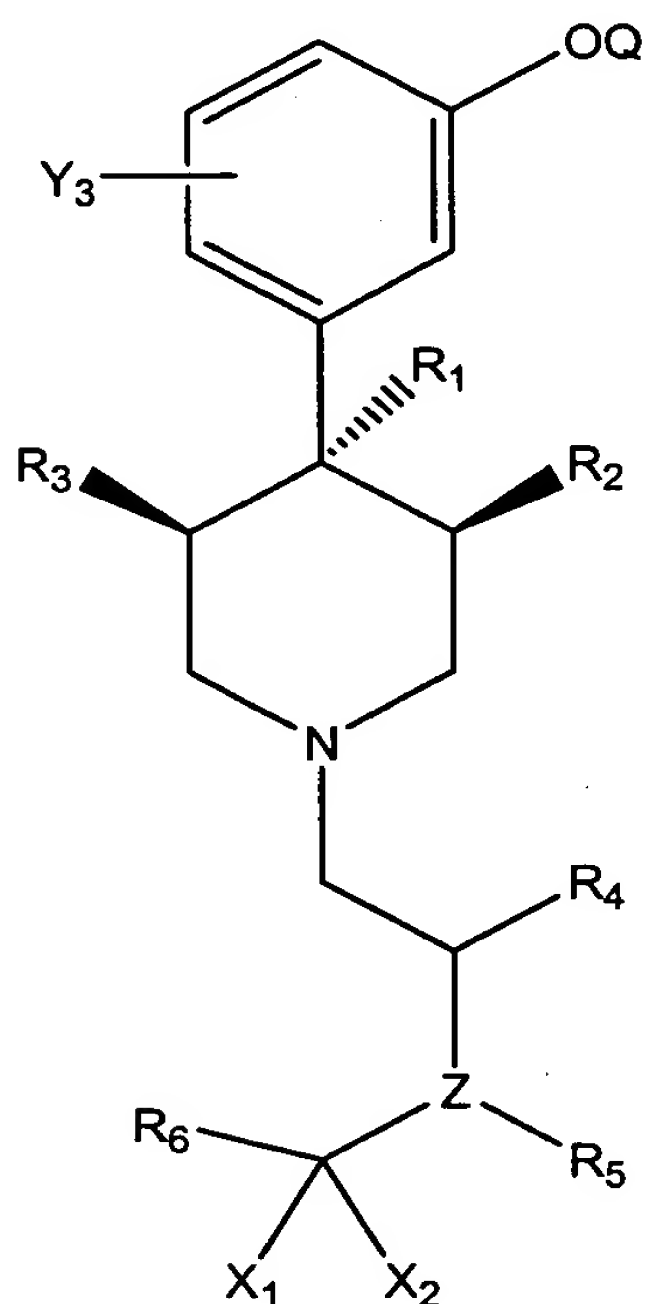
$R_6$  is a group having a formula selected from the group consisting of structures (a) and (b); and

$R_7$  is H,  $C_{1-8}$  alkyl,  $CH_2$ aryl substituted by one or more substituents  $Y_1$  or  $CH_2(CH_2)_nY_2$ .

Claim 12 (Original) The kappa opioid receptor antagonist of claim 7, wherein said compound is a compound selected from formulae 14-21 of Fig. 1.

Claim 13 (Currently Amended) A pharmaceutical composition comprising:  
an effective amount of a kappa opioid receptor antagonist and a physiologically acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula (I):

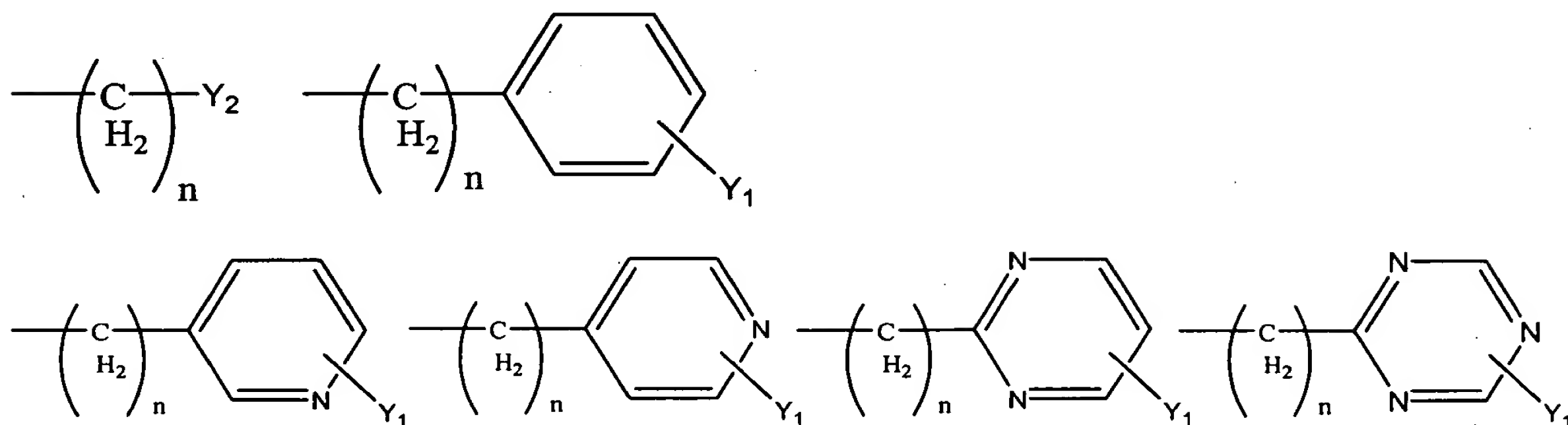




(I)

wherein Q is H or  $\text{COC}_{1-8}$  alkyl;

$R_1$  is  $\text{C}_{1-8}$  alkyl, or one of the following structures:



$\text{Y}_1$  is H, OH, Br, Cl, F, CN,  $\text{CF}_3$ ,  $\text{NO}_2$ ,  $\text{N}_3$ ,  $\text{OR}_8$ ,  $\text{CO}_2\text{R}_9$ ,  $\text{C}_{1-6}$  alkyl,  $\text{NR}_{10}\text{R}_{11}$ ,

$\text{NHCOR}_{12}$ ,  $\text{NHCO}_2\text{R}_{12}$ ,  $\text{CONR}_{13}\text{R}_{14}$ , or  $\text{CH}_2(\text{CH}_2)_n\text{Y}_2$ ;

$\text{Y}_2$  is H,  $\text{CF}_3$ ,  $\text{CO}_2\text{R}_9$ ,  $\text{C}_{1-6}$ alkyl,  $\text{NR}_{10}\text{R}_{11}$ ,  $\text{NHCOR}_{12}$ ,  $\text{NHCO}_2\text{R}_{12}$ ,  $\text{CONR}_3\text{R}_{14}$ ,

$\text{CH}_2\text{OH}$ ,  $\text{CH}_2\text{OR}_8$ , or  $\text{COCH}_2\text{R}_9$ ;

$Y_3$  is H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $OR_8$ ,  $CO_2R_9$ ,  $C_{1-6}$  alkyl,  $NR_{10}R_{11}$ ,  $NHCOR_{12}$ ,  $NHCO_2R_{12}$ ,  $CONR_{13}R_{14}$ , or  $CH_2(CH_2)_nY_2$ ;

$R_2$  is H,  $C_{1-8}$  alkyl,  $C_{3-8}$  alkenyl,  $C_{3-8}$  alkynyl or  $CH_2$ aryl substituted by one or more groups  $Y_1$ ;

$R_3$  is H,  $C_{1-8}$  alkyl,  $C_{3-8}$  alkenyl,  $C_{3-8}$  alkynyl or  $CH_2$ aryl substituted by one or more groups  $Y_1$ ;

wherein  $R_2$  and  $R_3$  may be bonded together to form a  $C_{2-8}$  alkyl group;

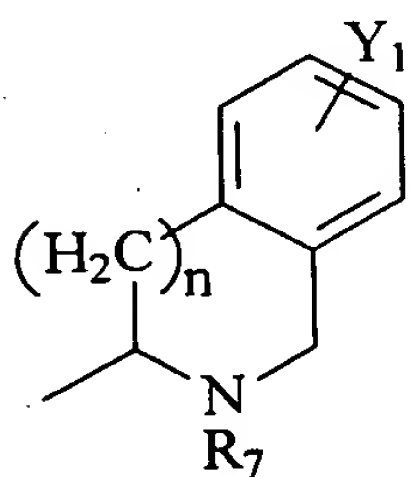
$R_4$  is hydrogen,  $C_{1-8}$  alkyl,  $CO_2C_{1-8}$  alkylaryl substituted by one or more groups  $Y_1$ ,  $CH_2$ aryl substituted by one or more groups  $Y_1$ , or  $CO_2C_{1-8}$  alkyl;

$Z$  is N, O or S; when  $Z$  is O or S, there is no  $R_5$

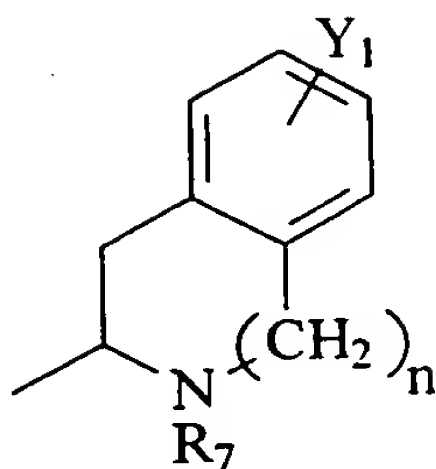
$R_5$  is H,  $C_{1-8}$  alkyl,  $C_{3-8}$  alkenyl,  $C_{3-8}$  alkynyl,  $CH_2CO_2C_{1-8}$  alkyl,  $CO_2C_{1-8}$  alkyl or  $CH_2$ aryl substituted by one or more groups  $Y_1$ ;

$n$  is 0, 1, 2 or 3;

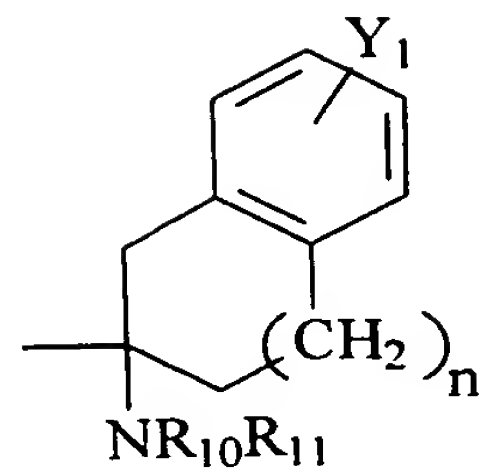
$R_6$  is a group selected from the group consisting of structures (a)-(bbb):



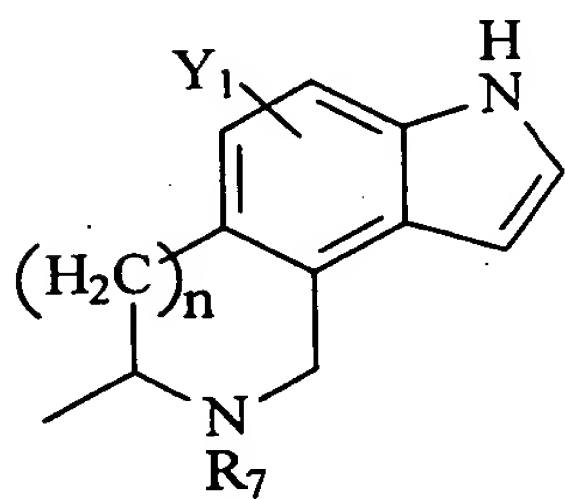
(a)



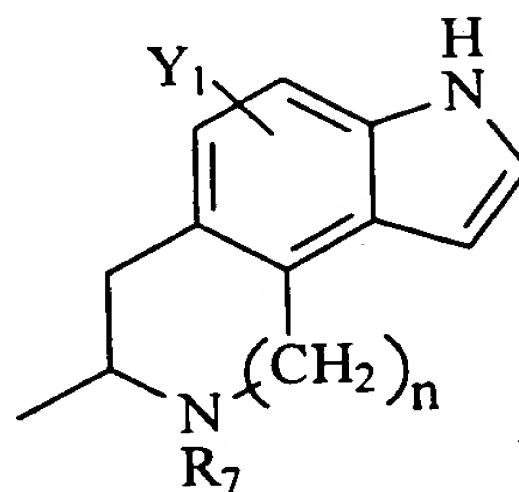
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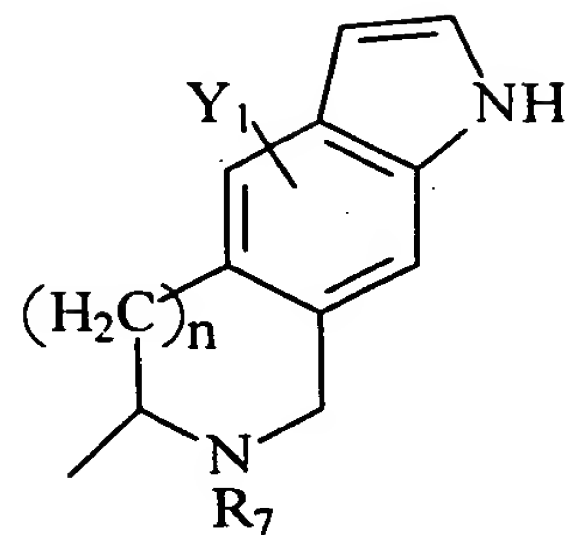
(c)



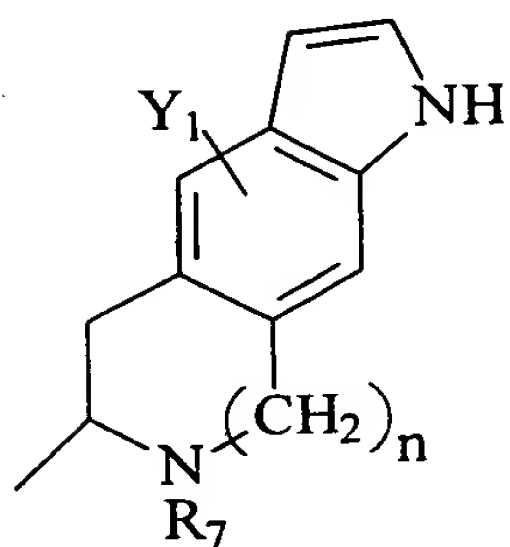
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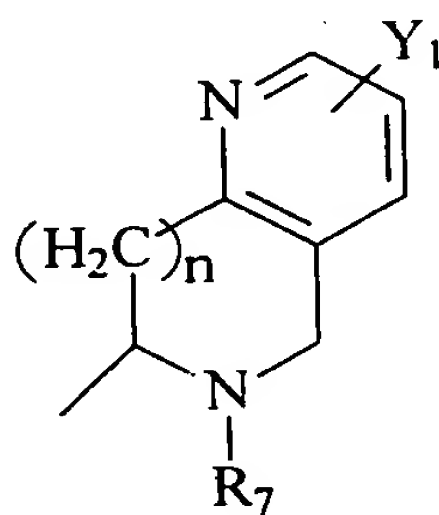
(e)



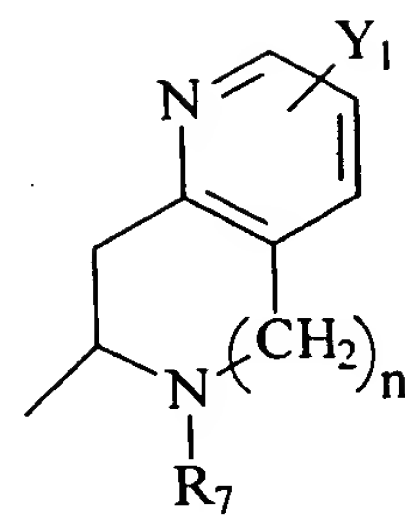
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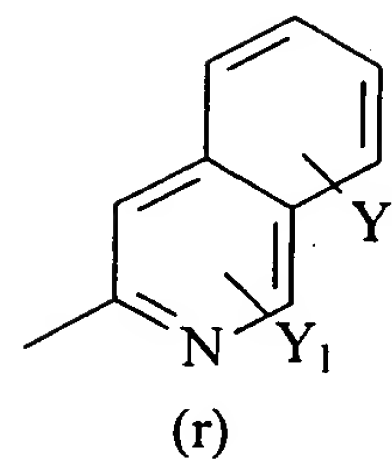
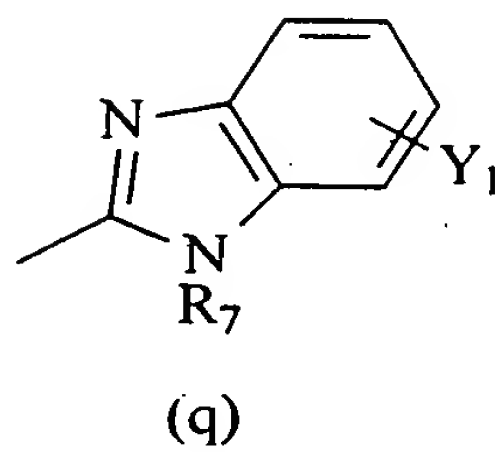
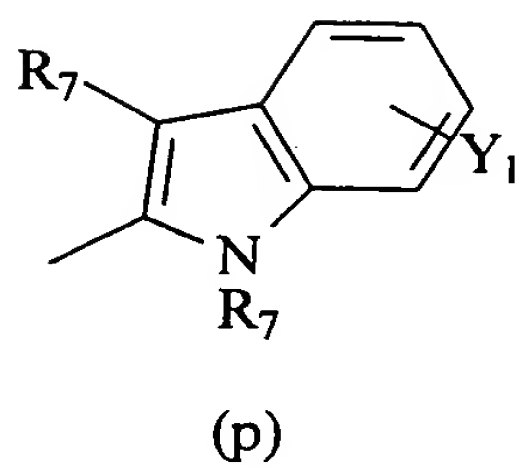
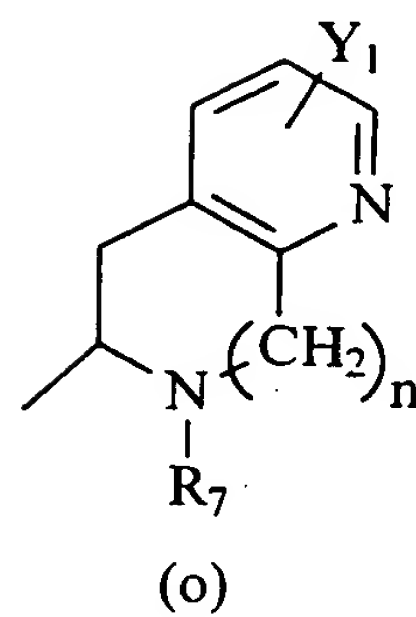
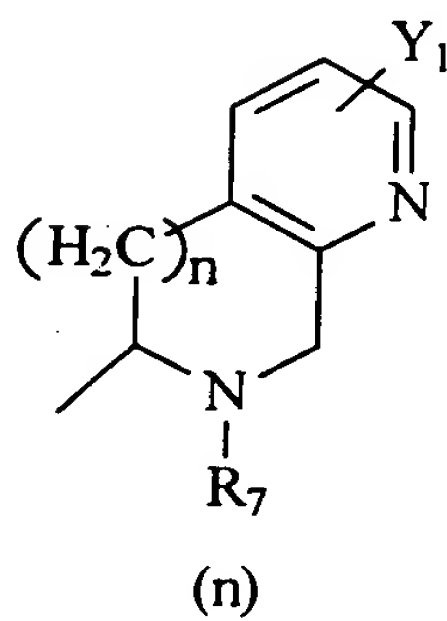
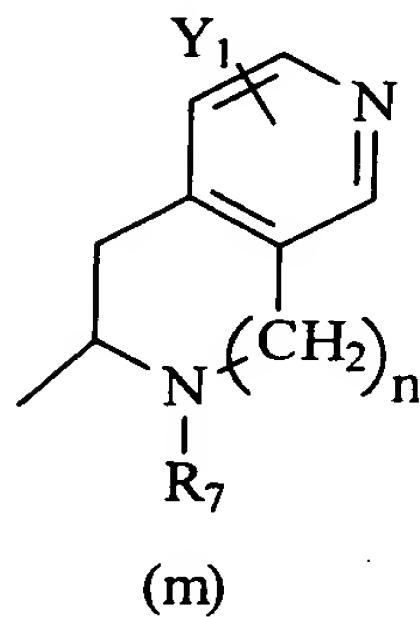
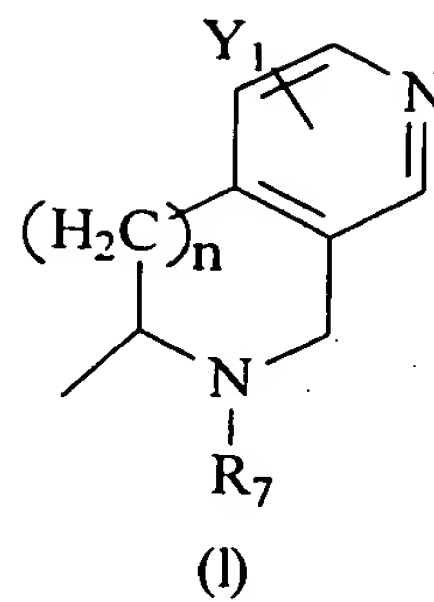
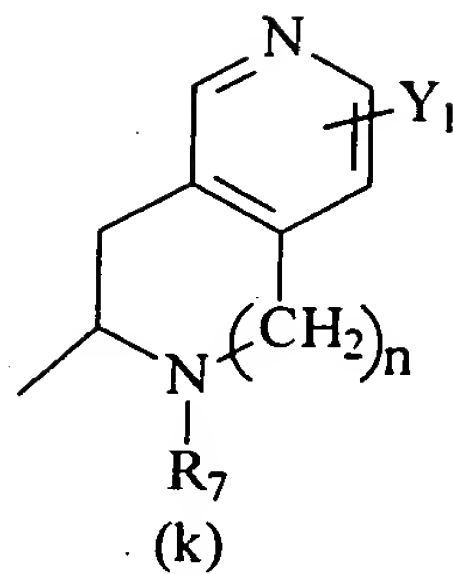
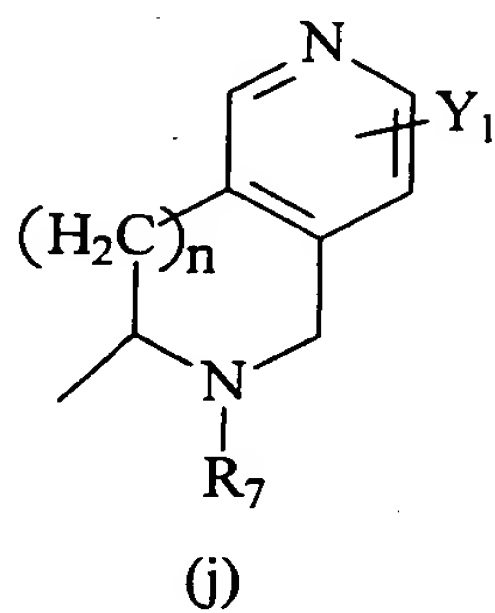
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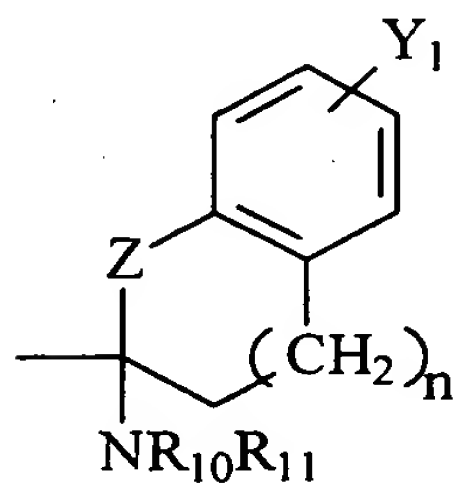


(h)

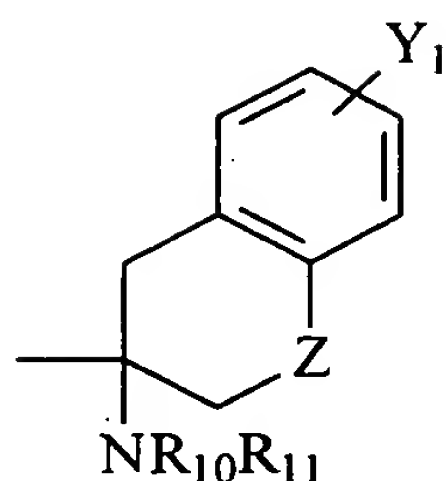


(i)

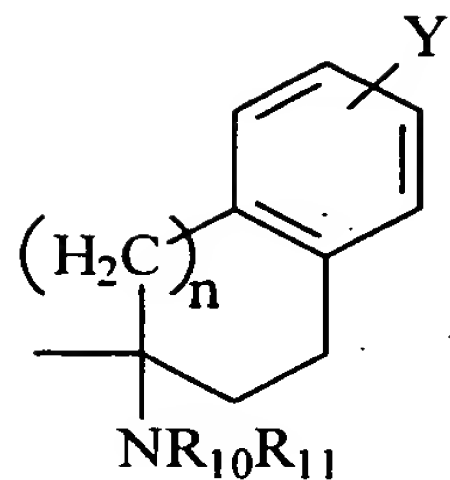




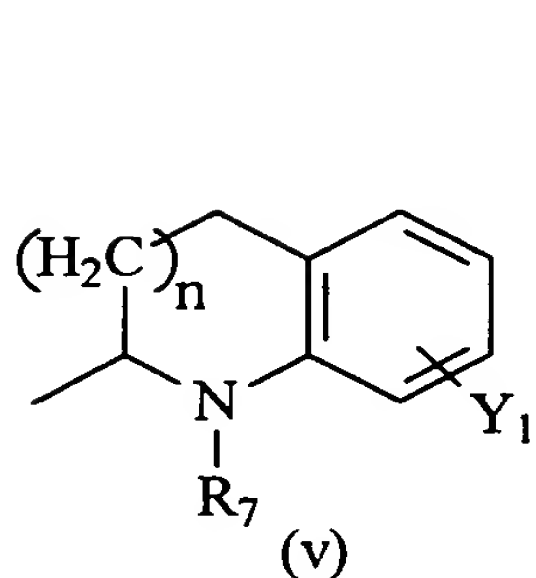
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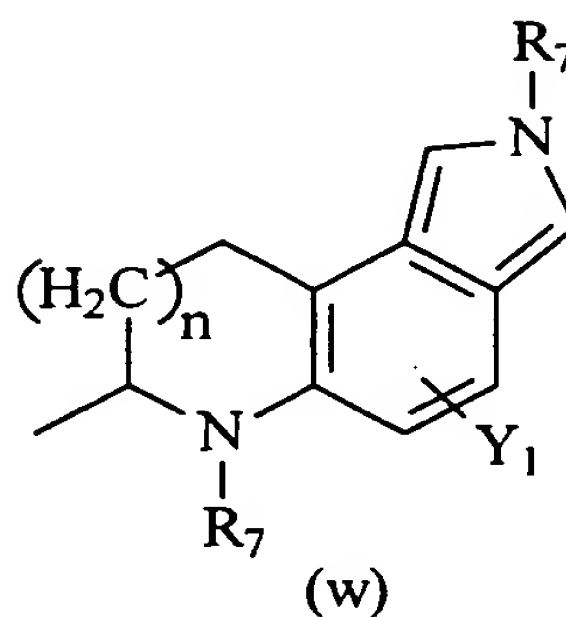
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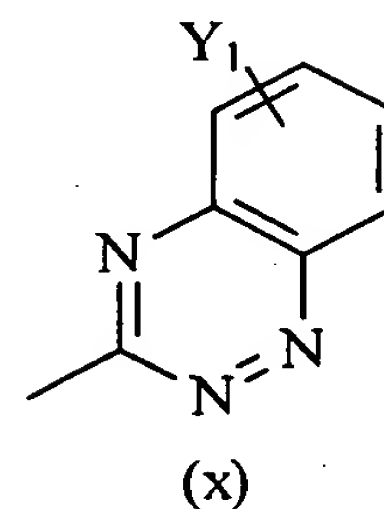
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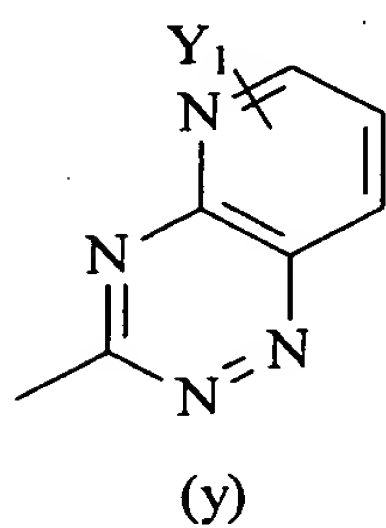
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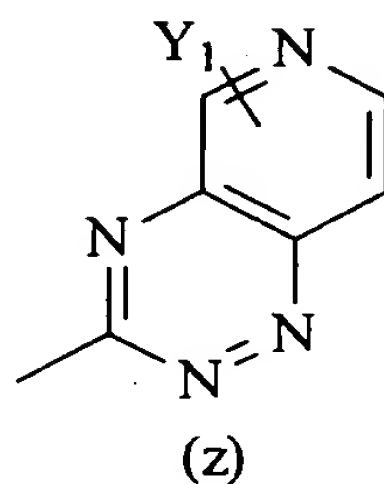
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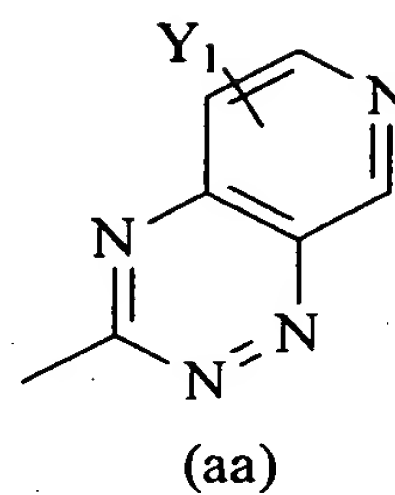
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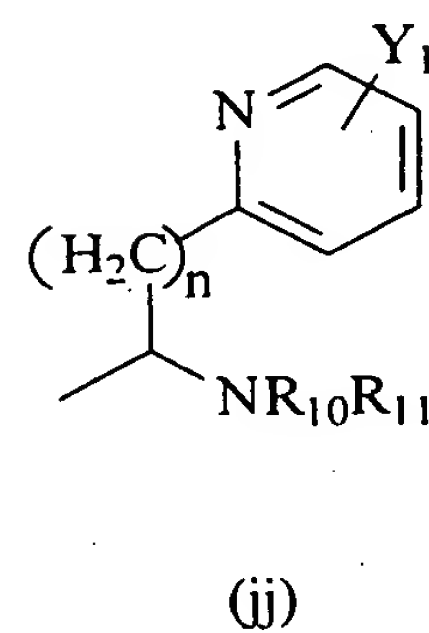
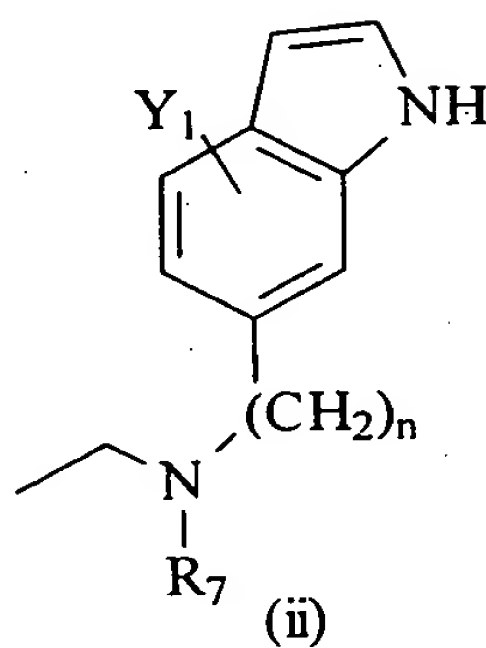
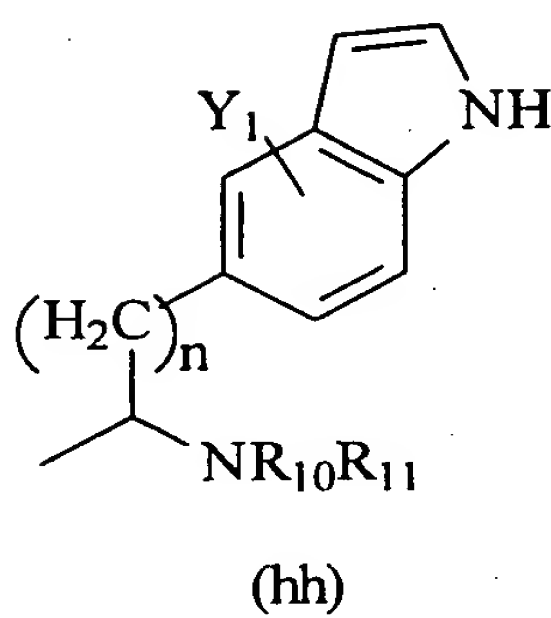
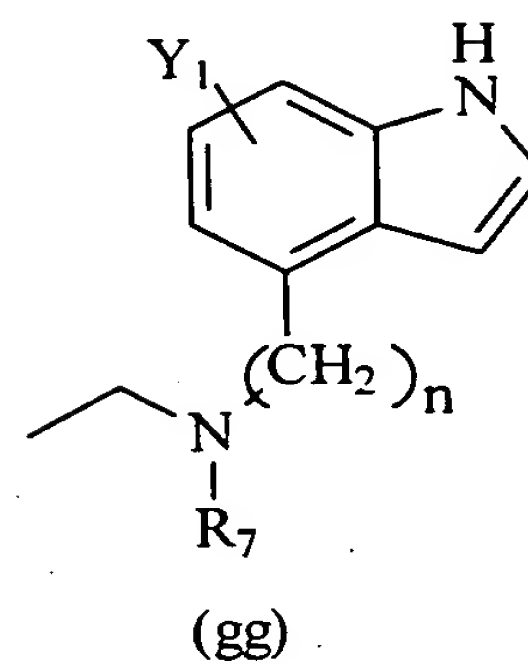
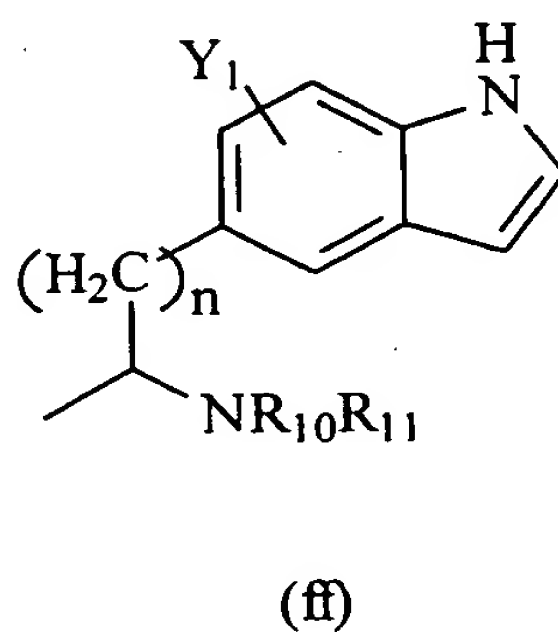
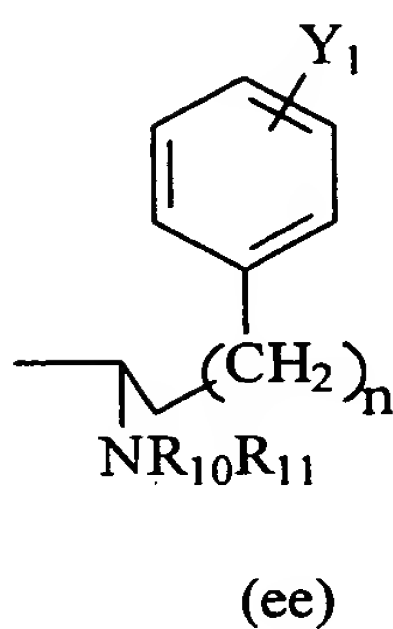
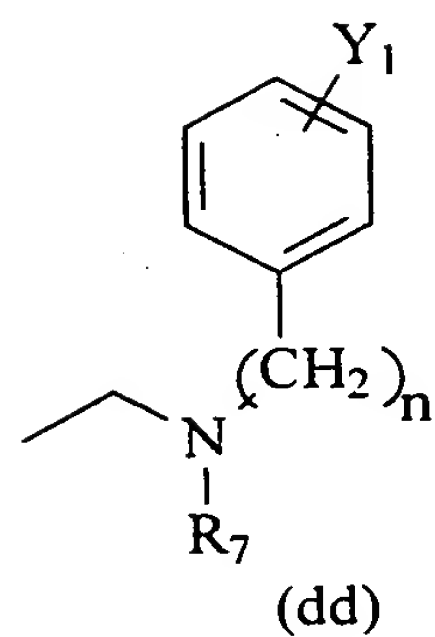
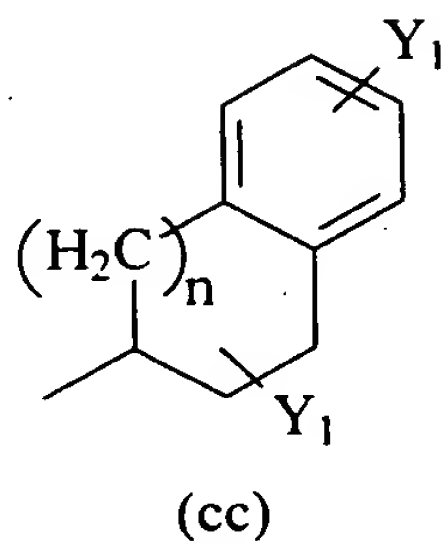
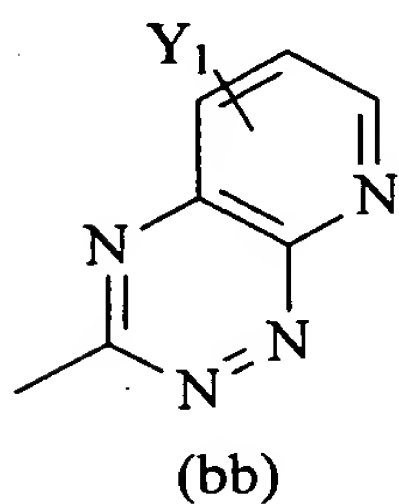
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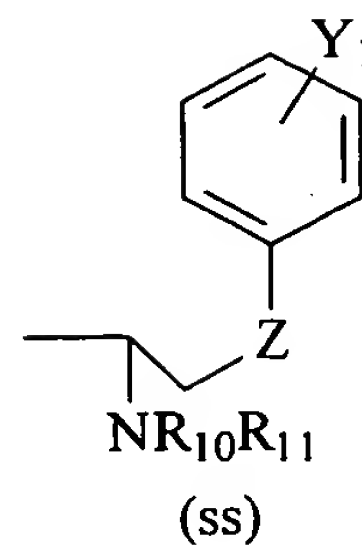
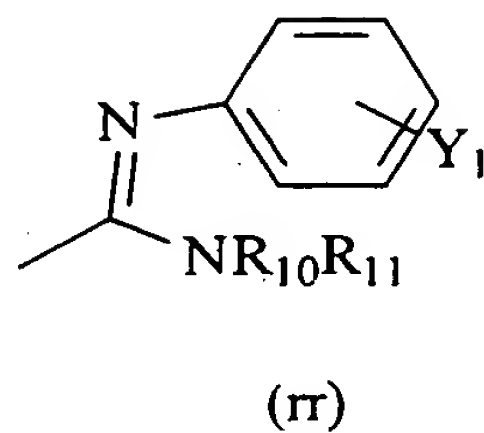
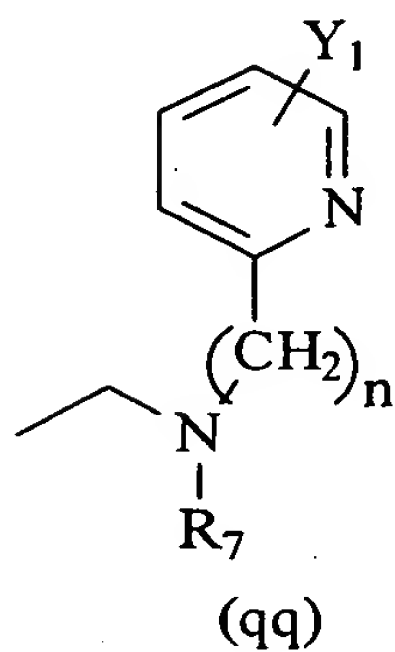
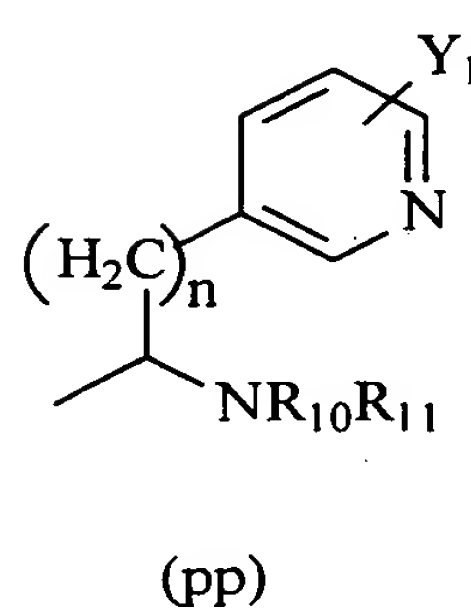
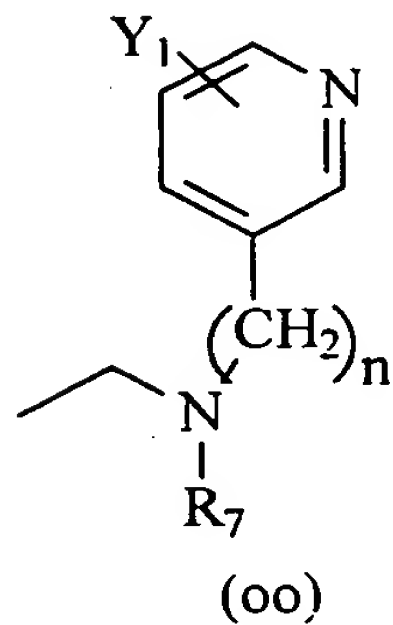
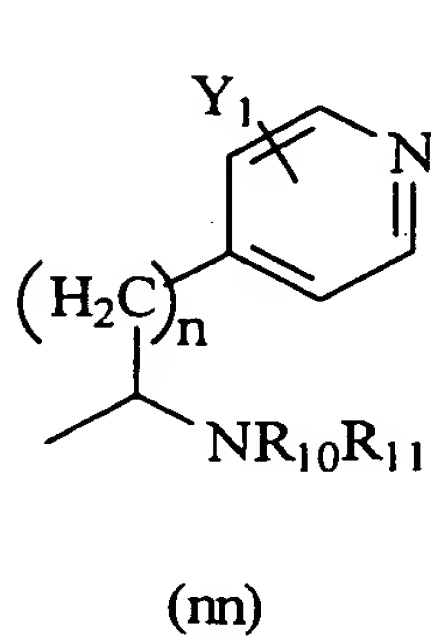
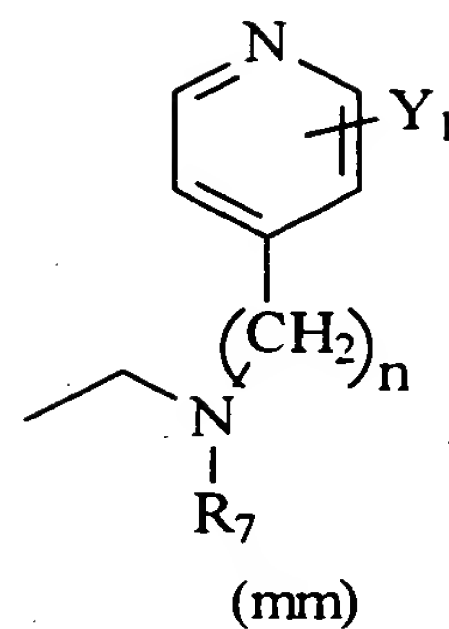
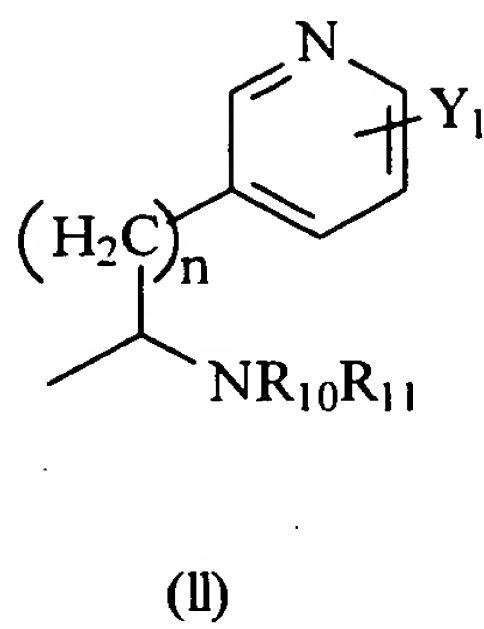
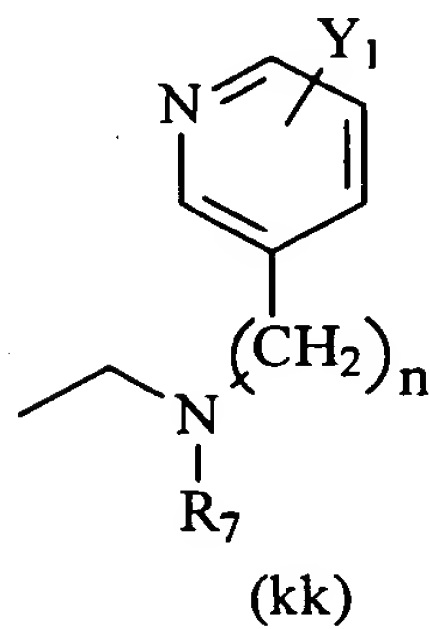


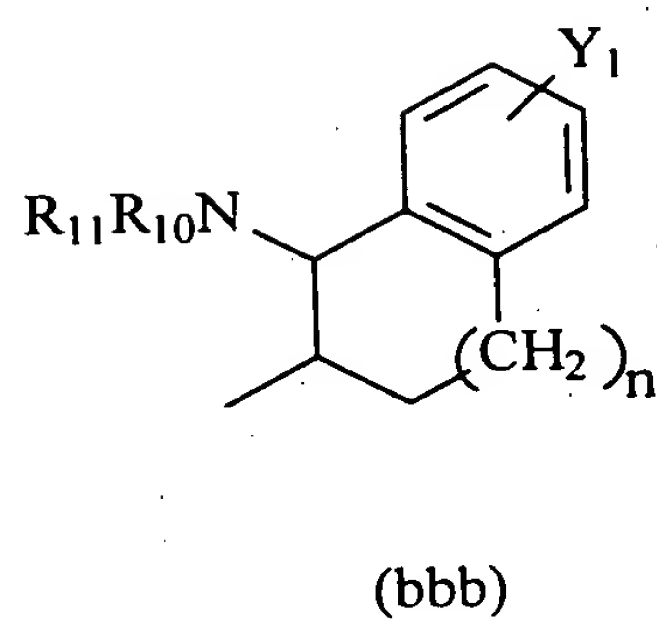
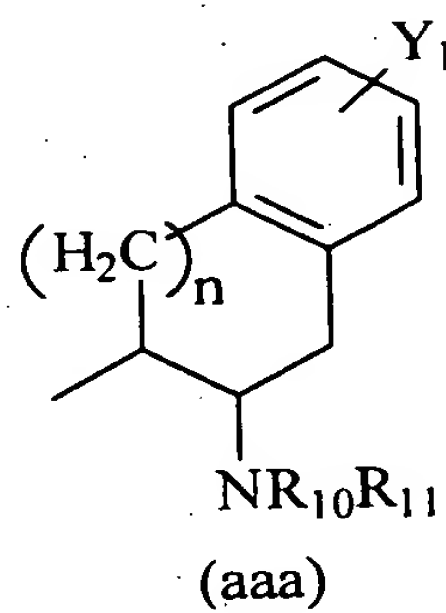
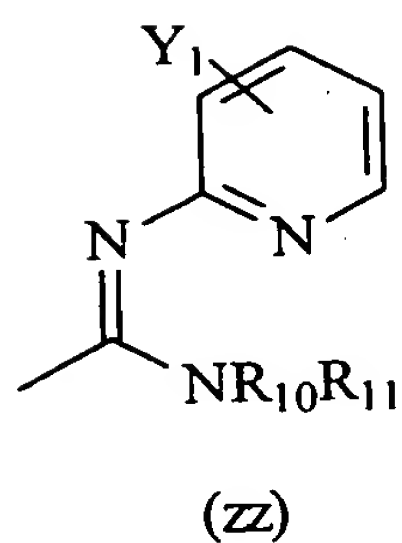
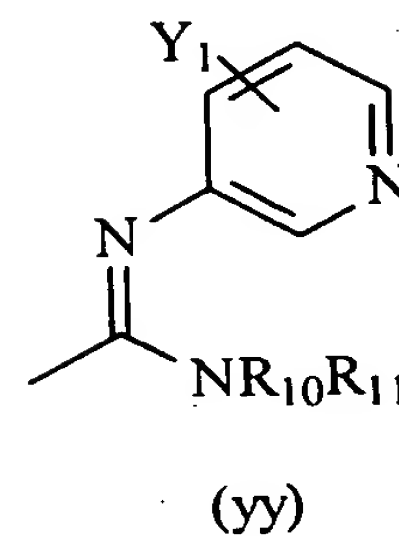
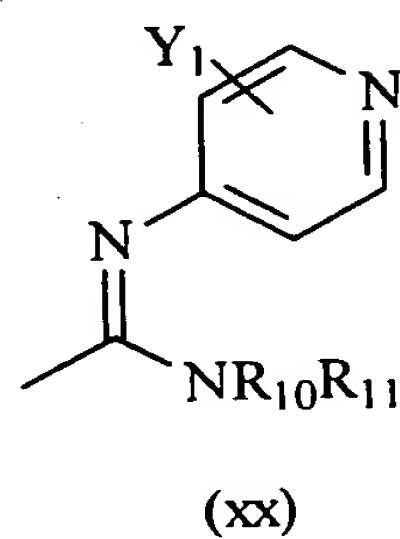
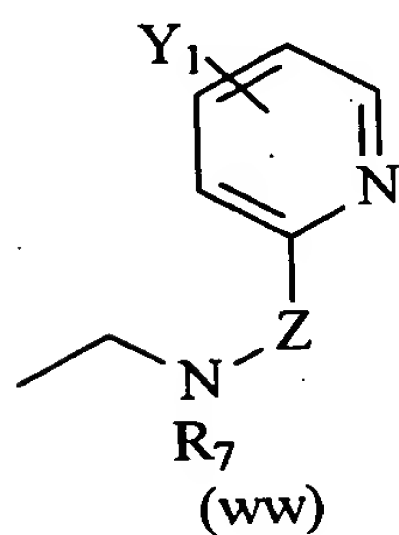
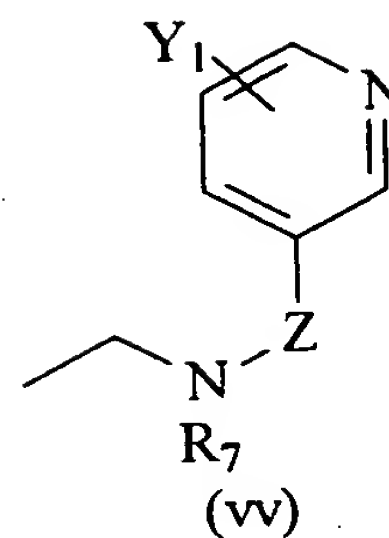
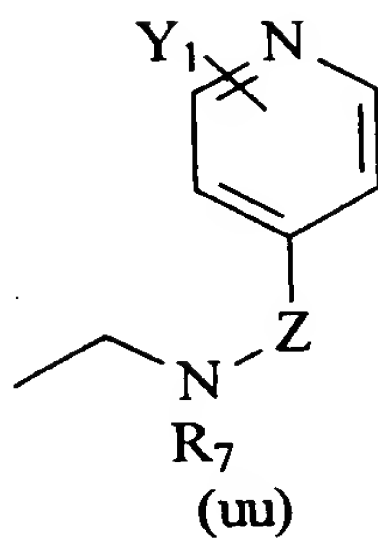
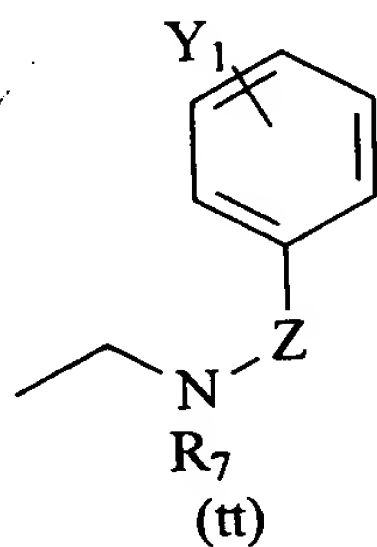
(z)



(aa)









$X_1$  is hydrogen,  $C_{1-8}$  alkyl,  $C_{3-8}$  alkenyl, or  $C_{3-8}$  alkynyl;

$X_2$  is hydrogen,  $C_{1-8}$  alkyl,  $C_{3-8}$  alkenyl, or  $C_{3-8}$  alkynyl;

or  $X_1$  and  $X_2$  together form  $=O$ ,  $=S$ ,  $=NH$ ;

$R_7$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_1$ ,  $NR_{10}R_{11}$ ,  $NHCOR_{12}$ ,  $NHCO_2R_{13}$ ,  $CONR_{14}R_{15}$ ,  $CH_2(CH_2)_nY_2$ , or  $C(=NH)NR_{16}R_{17}$ ;

$R_8$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_1$ ,  ~~$CONR_{13}R_{14}$~~  or  $CH_2(CH_2)_nY_2$ , H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_9$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_1$ , ~~or~~  $CH_2(CH_2)_nY_2$ , H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_{10}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_1$ , ~~or~~  $CH_2(CH_2)_nY_2$ , H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_{11}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_1$ , ~~or~~  $CH_2(CH_2)_nY_2$ , H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_{12}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_1$ , ~~or~~  $CH_2(CH_2)_nY_2$ , H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_{13}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_1$ , ~~or~~  $CH_2(CH_2)_nY_2$ , H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$  alkyl;

$R_{14}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_1$ , or  $CH_2(CH_2)_nY_2$ ; H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$ alkyl;

$R_{15}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_1$ , or  $CH_2(CH_2)_nY_2$ ; H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$ alkyl;

$R_{16}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_1$ , or  $CH_2(CH_2)_nY_2$ ; H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$ alkyl; and

$R_{17}$  is H,  $C_{1-8}$  alkyl,  $CH_2$  aryl substituted by one or more substituents  $Y_1$ , or  $CH_2(CH_2)_nY_2$ ; H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $C_{1-6}$  alkyl, or  $CH_2(CH_2)_nY_2'$ ; wherein  $Y_2'$  is H,  $CF_3$ , or  $C_{1-6}$ alkyl

or a pharmaceutically acceptable salt thereof.

Claim 14. (Previously Presented) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein  $R_1$ ,  $R_4$ ,  $R_5$ ,  $Y_1$ ,  $Y_2$ ,  $Z$ ,  $n$ ,  $X_1$ ,  $X_2$ , and  $R_7$ - $R_{17}$  are as in Claim 13;

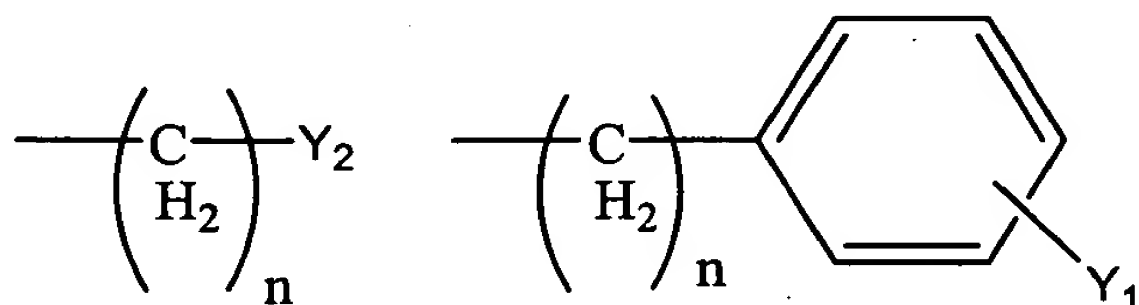
$Y_3$  is H;

$R_2$  and  $R_3$  are each, independently, H,  $C_{1-8}$  alkyl,  $C_{3-8}$  alkenyl,  $C_{3-8}$  alkynyl, or  $CH_2$ aryl substituted by one or more substituents  $Y_1$ ; and

$R_6$  is a group having a formula selected from the group consisting of structures (a)-(cc).

Claim 15. (Previously Presented) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (1), wherein  $Y_1$ ,  $Y_2$ ,  $R_4$ ,  $R_5$ ,  $Z$ ,  $n$ ,  $X_1$ ,  $X_2$  and  $R_8$ - $R_{15}$  are as in Claim 13;

$R_1$  is  $C_{1-8}$  alkyl, or one of the following structures:



$Y_3$  is H;

$R_2$  and  $R_3$  are each, independently, H or  $C_{1-8}$  alkyl, wherein  $R_2$  and  $R_3$  cannot both be H at the same time;

$R_6$  is a formula selected from the structures (a)-(r) shown above; and

$R_7$  is H,  $C_{1-8}$  alkyl,  $\text{CH}_2$ aryl substituted by one or more substituents  $Y_1$ ,  $\text{NR}_{10}\text{R}_{11}$ ,  $\text{NHCOR}_{12}$ ,  $\text{NHCO}_2\text{R}_{13}$ ,  $\text{CONR}_{14}\text{R}_{15}$ , or  $\text{CH}_2(\text{CH}_2)_n\text{Y}_2$ .

Claim 16. (Previously Presented) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein  $Y_1$ ,  $Z$ ,  $n$ ,  $X_1$ ,  $X_2$  and  $R_8$ - $R_{15}$  are as noted- above in Claim 13;

$R_1$  is  $C_{1-8}$  alkyl;

$Y_2$  is H,  $\text{CF}_3$ ,  $\text{CO}_2\text{R}_9$ ,  $C_{1-6}$  alkyl,  $\text{NR}_{10}\text{R}_{11}$ ,  $\text{NHCOR}_{12}$ ,  $\text{NHCO}_2\text{R}_{12}$ ,  $\text{CONR}_{13}\text{R}_{14}$ ,  $\text{CH}_2\text{OH}$ ,  $\text{CH}_2\text{OR}_8$ , or  $\text{COCH}_2\text{R}_9$ ;

$Y_3$  is H;

$R_2$  and  $R_3$  are each, independently, H or methyl, wherein  $R_2$  and  $R_3$  cannot both be H at the same time;

$R_4$  is H,  $C_{1-8}$  alkyl,  $\text{CO}_2\text{C}_{1-8}\text{alkyl}$ , or  $\text{CH}_2$  aryl substituted by one or more substituents  $Y_1$  and the stereocenter adjacent to  $R_4$  is in an (S) configuration;

R<sub>5</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub>CO<sub>2</sub>C<sub>1-8</sub> alkyl;

R<sub>6</sub> is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

R<sub>7</sub> is H, C<sub>1-8</sub>alkyl, CH<sub>2</sub>aryl substituted by one or more substituents Y<sub>1</sub>, NR<sub>10</sub>R<sub>11</sub>, NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>13</sub>, CONR<sub>14</sub>R<sub>15</sub>, or CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

Claim 17. (Previously Presented) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (1), wherein Y<sub>1</sub>, Z, n, X<sub>1</sub>, X<sub>2</sub> and R<sub>8</sub>-R<sub>14</sub> are as in Claim 13;

R<sub>1</sub> is methyl,

Y<sub>2</sub> is H, CF<sub>3</sub>, CO<sub>2</sub>R<sub>9</sub>, C<sub>1-6</sub> alkyl, NR<sub>10</sub>R<sub>11</sub>, NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>12</sub>, CONR<sub>13</sub>R<sub>14</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>OR<sub>8</sub>, or COCH<sub>2</sub>R<sub>9</sub>;

Y<sub>3</sub> is H;

R<sub>2</sub> and R<sub>3</sub> are each H or methyl, such that when R<sub>2</sub> is H, R<sub>3</sub> is methyl and vice versa;

R<sub>4</sub> is C<sub>1-8</sub> alkyl, or CO<sub>2</sub>C<sub>1-8</sub> alkyl, and the stereocenter adjacent to R<sub>4</sub> has a configuration of (S);

R<sub>5</sub> is H;

R<sub>6</sub> is a group having a formula selected from the group consisting of structures (a) and (b); and

R<sub>7</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub>aryl substituted by one or more substituents Y, or CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

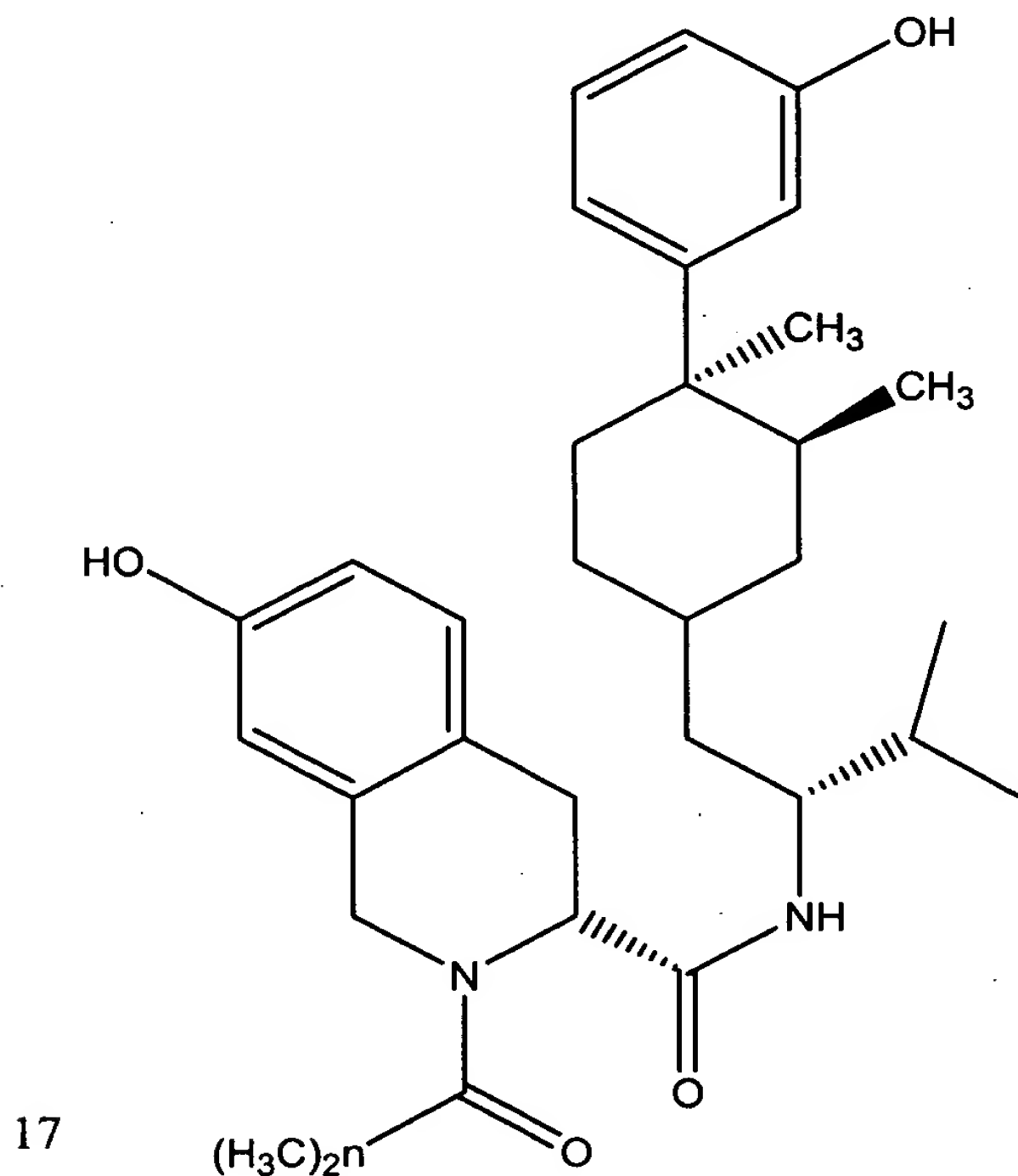
Claim 18. (Original) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound selected from formulae 14-21 of Fig. 1.

Claim 19. (Original) The pharmaceutical composition of claim 13, wherein said composition is an injectable composition.

Claim 20. (Original) The pharmaceutical composition of claim 13, wherein said composition is an orally administrable composition.

Claim 21. (Original) The pharmaceutical composition of claim 20, wherein said orally administrable composition is in a form selected from the group consisting of tablets, capsules, troches, powders, solutions, dispersions, emulsions and suspensions.

Claim 22. (Previously Presented) The kappa opioid receptor antagonist according to Claim 7, having the chemical formula:



Claim 23. (Previously Presented) The method of binding a kappa opioid receptor in a subject in need thereof, as claimed in claim 1, wherein  $R_1$  is  $C_{1-8}$ alkyl;  $(CH_2)_n-Y_2$ ;  $(CH_2)_n$ -phenyl- $Y_2$ ; or  $(CH_2)_n$ -pyridyl- $Y_1$ , and  $R_6$  is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb), and wherein Q,  $Y_1$ - $Y_3$ ,  $R_2$ - $R_5$ , Z, n,  $X_1$ ,  $X_2$ , and  $R_7$ - $R_{17}$  are as in Claim 1.

Claim 24. (Previously Presented) The kappa opioid receptor antagonist compound as claimed in claim 7, wherein  $R_1$  is  $C_{1-8}$ alkyl;  $(CH_2)_n-Y_2$ ;  $(CH_2)_n$ -phenyl- $Y_1$ ; or  $(CH_2)_n$ -pyridyl- $Y_1$ , and  $R_6$  is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb), and wherein Q,  $Y_1$ - $Y_3$ ,  $R_2$ - $R_5$ , Z, n,  $X_1$ ,  $X_2$ , and  $R_7$ - $R_{17}$  are as in Claim 7.

Claim 25. (Previously Presented) The pharmaceutical composition as claimed in claim 13, wherein  $R_1$  is  $C_{1-8}$ alkyl;  $(CH_2)_n-Y_2$ ;  $(CH_2)_n$ -phenyl- $Y_1$ ; or  $(CH_2)_n$ -pyridyl- $Y_1$ , and  $R_6$  is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb), and wherein Q,  $Y_1$ - $Y_3$ ,  $R_2$ - $R_5$ , Z, n,  $X_1$ ,  $X_2$ , and  $R_7$ - $R_{17}$  are as in Claim 13.